A Dissertation on

CORRELATIVE STUDY OF CAROTID INTIMA MEDIA THICKNESS AND VARIOUS CORONARY RISK FACTERS IN TYPE 2 DIABETICS WITH AND WITHOUT CORONARY ARTERY DISEASE

COIMBATORE MEDICAL COLLEGE HOSPITAL

COIMBATORE

A Dissertation Submitted to

THE TAMILNADU DR.M.G.R.MEDICAL UNIVERSITY

CHENNAI – 600032

with partial fulfillment of the regulations
for the award of the degree of

M.D.GENERAL MEDICINE

BRANCH - I

COIMBATORE MEDICAL COLLEGE
COIMBATORE
APRIL – 2016

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This is to certify that the dissertation entitled **"CORRELATIVE STUDY OF CAROTID INTIMA MEDIA THICKNESS AND VARIOUS CORONARY RISK FACTERS IN TYPE 2 DIABETICS WITH AND WITHOUT CORONARY ARTERY DISEASE**" is a bonafide research work done by Dr. SURESH.M, Post Graduate student in General Medicine, under my direct guidance and supervision. This is being submitted to the The Tamil Nadu Dr. M.G.R. Medical University, Chennai, in partial fulfillment of the regulations for the award of M.D. Degree in General Medicine examination to be held in April 2016. I have great pleasure in forwarding the same to The Tamil Nadu Dr. M.G.R. Medical University, Chennai, Tamilnadu, India.

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I, **Dr. SURESH.M** hereby declare that this dissertation entitled **"CORRELATIVE STUDY OF CAROTID INTIMA MEDIA THICKNESS AND VARIOUS CORONARY RISK FACTERS IN TYPE 2 DIABETICS WITH AND WITHOUT CORONARY ARTERY DISEASE**". is a bonafide and genuine research work carried out by me under the guidance of **Prof. Dr.M.RAVEENDRAN, M.D.**, Department of Medicine, Coimbatore Medical College, Coimbatore, in partial fulfillment of the regulations for the award of M.D. Degree in General Medicine to be held in Apr 2016.

This dissertation has not been submitted by me on any previous occasion to any university for the award of any degree.

Date:----------
Place: Coimbatore

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LIST OF ABBREVIATIONS USED

CIMT	–	Carotid Intima Media Thickness
IMT	–	Intima Media Thickness
Type 2 DM	–	Type 2 Diabetes Mellitus
HTN	–	Hypertension
HbA1C	–	glycosylated Haemoglobin BMI – Body Mass Index
W/ H Ratio	–	Waist Hip Ratio
IHD	–	Ischemic Heart Disease
CAD	–	Coronary Artery Disease
Total C	–	Total Cholesterol
HDL –C	-	High Density Lipo protein Cholesterol
LDL-C	–	Low Density Lipo protein Cholesterol
TG	–	Triglycerides
M.I.	–	Myocardial Infarction
DBP	–	Diastolic Blood Pressure
SBP	–	Systolic Blood Pressure
FBS	–	fasting blood sugar
PPBS	–	post prandial blood sugar
ARIC	–	Atherosclerosis Risk In Communities
ARYA	–	Atherosclerosis Risk in Young Adults
OHA	–	Oral Hypoglycemic Agents
CCA	–	Common Carotid Artery
ICA	–	Internal Carotid Artery

Rx	–	treatment
IGT	–	Impaired Glucose Tolerance
FTG	–	Fasting Triglyceride
PPTG	–	Post prandial Triglyceride

INTRODUCTION

Diabetic patients are more prone for early atherosclerotic changes. Multiple studies shows that diabetic patients have a high value of lipids and most of them suffering from obesity, hypertension, which leads to metabolic syndrome and its consequences like coronary artery heart disease, cerebrovascular accident and peripheral vascular disease.[1]

Epidemiological studies have established certain factors,(male person, age, dyslipidemia, diabetes, hypertension, and smoking) as predictors of clinical manifestations of coronary artery disease (CAD).[2-4] Above said risk factors have also, well correlated with the presence and extent of CAD documented by coronary angiography.[5-7] Efforts to predict the presence as well as extent of CAD at angiography on the basis of risk factors, however, have been variably successful.[8-10] Imaging of peripheral arteries like carotid artery has been suggested as a means of increasing predictive ability for CAD beyond that of traditional risk factor models. Non colour or B mode ultrasonography of the extracranial carotid arteries offers repeatable, non-invasive method for quantifying the extent of atherosclerosis.[11-13] Therefore B mode ultrasonography of peripheral vessels such as carotid artery imaging introduced in 1980s, to evaluate atherosclerotic lesions and their progression.[14,15] which is an alternative to angiography

Ultrasound imaging of carotid vessels gives information about CIMT, presence or absence plaques and nature and types of plaques, wall thickness,

calcification, pre-symptomatic lesion and it is also used to evaluate the atherosclerotic burden and risk of cardiovascular events. It is a non invasive imaging modality, more useful to identify the risk of coronary artery disease in diabetic patients and also facilitate, early intervention in clinical setting.

The cardiovascular health study collaborative research group[3] has studied in 4476 patients without clinical cardiovascular disease for the period of 6 years followup, they noticed that the relative risk of coronary artery heart disease or cerebrovascular accident for the quantile with the highest CIMT as compare with the lowest quantile was 3.87. [17]

Compare to the other traditional risk factors , The CIMT is a very strong surrogate tool for identifying new cardiovascular accidents, even after adjustment with statistics. In a case control study, 772 candidates choosed from the Atherosclerosis Risk In Communities population to evaluate clinical cardiovascular disease. The case as well as the control groups selected by CIMT. The study group shows, high values of coronary risk factors (age, SBP, DBP, BMI , smoking, , low-density lipoprotein (LDL cholesterol), total triglycerides, total cholesterol and low value of high density lipoprotein (HDL cholesterol) than control group.[18]

In Indian subjects, Carotid Intima Media Thickness was independently associated with CAD.[19] But, few numbers of Indian studies available about carotid intima-medial thickness evaluation in type 2 diabetics with and without coronary artery disease. So, this study was planned to generate more number of

data about CIMT and other various coronary risk factors in type 2 diabetics with or without CAD, as these patients are more prone to develop early atherosclerosis and have macro vascular complications like coronary artery disease. Non invasive procedures like, B mode ultrasonography of carotid vessels is used as predictor of early atherosclerosis, which is suggestive of coronary atherosclerosis in diabetic patients.

AIMS AND OBJECTIVES

1. To study the carotid intima media thickness in type 2 diabetics with coronary artery disease and without coronary artery disease.

2. To Correlate carotid intima media thickness with various coronary risk factors (age, sex, smoking, duration of diabetes, BMI, SBP,etc)

REVIEW OF LITERATURE

1. Atherosclerosis
2. Atherosclerotic factors influencing intima media thickness
3. Evaluation of CIMT by Doppler ultrasound- an indication of atherosclerosis
4. Anatomy of carotid arteries
5. Diabetes mellitus
6. Role of diabetes and insulin in atherosclerosis

Atherosclerosis

The major cause of death and premature morbidity in developed, as well as, in developing countries is due to atherosclerosis. The leading cause of total disease burden in worldwide is cardiovascular diseases mainly atherosclerosis by the year 2020. Although various generalized or systemic factors leads to its development, atherosclerosis involves different regions of the circulations, and produce various clinical manifestations based on, which circulation system is involved. [29]

Pathogenesis of atherosclerosis

Atherosclerosis is a multifactorial disease, in which, exact cause is not known. Several mechanisms have been putworth to delineate the pathogenesis of atherosclerosis, and the most popular being the "response to injury theory".[30]

The sequential components of the “response to injury” theory are as follows:

Endothelial injury

↓

Intimal smooth muscle cell proliferation

(Due to adherence of platelets, and platelets aggregation in sub endothelial connective tissue) ↓

Role of macrophages

Macrophages process accumulation of intracellular macrophages / foam cells)

↓

Role of Hyperlipidema

(Hyperlipidema may itself initiate endothelial injury and also promote the formation of foam cells) ↓

Thrombosis

(Platelet aggregation at site of endothelial injury causes proliferation of smooth muscle cells. atheroma plaque is formed by foam cells mixing with proliferated smooth muscle cells. The size of the plaque is increased by attachment of fibrin and blood cells thats leads to thrombus formation

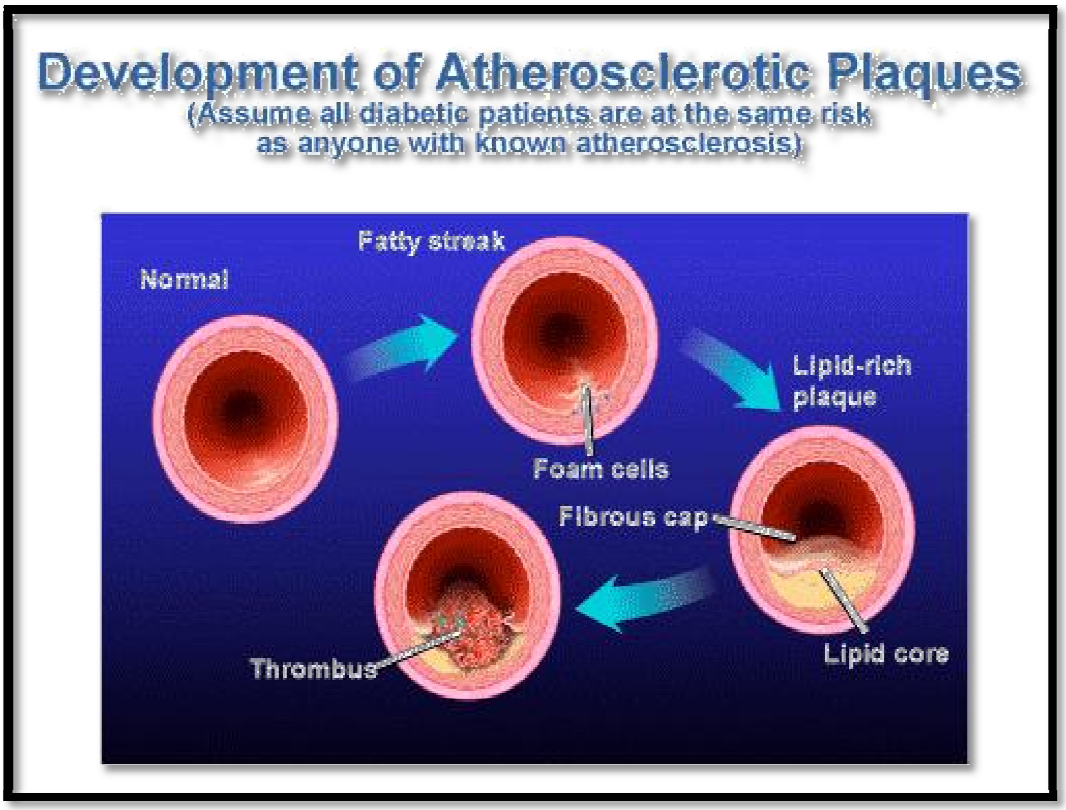


Figure -1 : Development of Atherosclerotic Plaques

Pathologic changes in atherosclerosis:

1. Intimal thickening:

The lesion consists of smooth muscle cells, fibrous tissue and some collagen, but no lipid.

2. Fatty streaks:

They are composed of closely packed foam cells, lipid containing elongated smooth muscle cells and a few lymphoid cells. Small amount of extra cellular lipid, collagen and proteoglycans are also present. They are considered to be the precursors of plaques.

3. Gelatinous lesions:

These are foci of increased ground substance in the intima with thinned overlying endothelium. They are also considered to be the precursors of plaques.

4. Atheromatous plaques:

A fully developed atheromatous lesion is called an atheromatous plaque.

- The plaque has a superficial fibrous cap – formed by proteoglycans, smooth muscle cells, collagen and dense connective tissue

- The cellular area under the fibrous cap is comprised of a mixture of macrophages, foam cells, lymphocytes and a few smooth muscle cells.
- The deeper central soft core consists of extra cellular lipid material, cholesterol clefts, fibrin, necrotic debris and lipid laden foam cells.

5. **Complicated plaques:**

Various complications can occur in fully developed lesions. These include calcification, ulceration, thrombosis, haemorrhage and aneurysm formation.

ATHEROSCLEROTIC FACTORS INFLUENCING INTIMA –MEDIA THICKNESS

1. Type-2 diabetes mellitus:

- Type-2 Diabetes Mellitus is known to be a predisposing factor of atherosclerosis. [31-34] Studies have confirmed that diabetic patients have an IMT greater than non diabetic individuals. Increased IMT in diabetes is independent of the other established risk factors.[16]

Chronic hyperglycemia is the causative agent for increased IMT in diabetic patients. This fact is proved by

- Those who have increased IMT, also have poorly controlled diabetic status and / or high duration of illness which leads to higher rates of coronary artery complications.[35,36]

- It is suggested that hyperglycemia is not a determinant of cardiovascular disease in Type-2 Diabetes but , both the conditions may share common antecedents such as insulin resistance, hyperinsulinemia, or genetic susceptibility.[35]

2. Lipid profile:

- High HDL cholesterol is negatively associated with IMT whereas high LDL cholesterol has a positive association.[16]

- postprandial hypertriglyceridemia is a major risk factor for high carotid IMT compared to normal FTG levels.

  Furthermore, PPTG is one of the independent risk factor for atherosclerosis and coronary artery heart disease. The cutoff value for PPTG levels is > 2.27 mmol/l.[37] above which, the tendency of increased CIMT is high

- Inspite of, there is no clear cut threshold level of PPTG for atherosclerosis, the cutoff value for PPTG levels is > 2.27 mmol/l , may be considered as postprandial hypertriglyceridemia. [37]

- In a study conducted in 1996, Alesa et al concluded that majority of young patients with hypercholesterolemia have a greater carotid intima media thickness than healthy subjects.[38]

3. Age:

Atherosclerosis is an age related disease.[16,39,40] Early lesions may be present in childhood, however clinically significant lesions are found with increasing age. Fully developed plaques usually appear in the fourth decade and beyond. Several studies have shown a positive correlation between age and CIMT.[41]

4.Sex:

Incidence and severity of atherosclerosis is more in men than in women.[32] Prevalence of atherosclerotic IHD is about three times higher in men in fourth decade than in women.

5. Genetic factors:

There is a familial disposition to atherosclerosis, which may be related to diabetes mellitus, hypertension and hyperlipoproteinemia.[32,42]

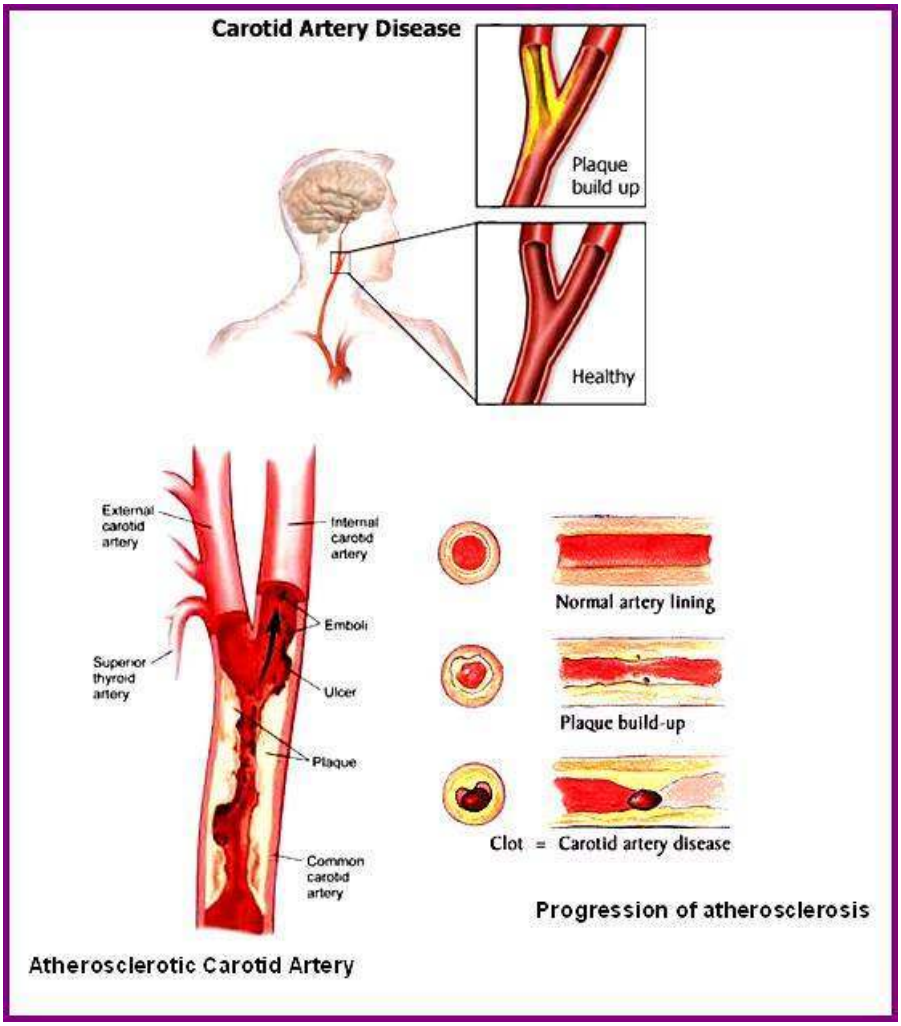


Figure -2: Progression of atherosclerosis in carotid artery

6. Hypertension:

Hypertension is a major risk factor in the development of atherosclerotic diseases like IHD and cerebrovascular disease.[39,43] A systolic pressure above 160 mmHg or a diastolic pressure of over 95 mmHg is associated with five times higher risk.

7. Geographical factors:

There is a high incidence of atherosclerosis in the United States, Europe and Australia and a low prevalence in underdeveloped countries.[44]

8. Diet:

Saturated fats like eggs, meat, milk etc, tend to raise plasma cholesterol levels and predispose to atherosclerosis. On the contrary, a diet rich in poly-unsaturated fats (e.g. fish, fish oils etc) lowers the plasma cholesterol levels and has beneficial effects.[44]

9. Smoking:

Smoking can aggravate atherosclerosis.[39,43] Increased risk of atherosclerosis in smokers is mainly due to reduced levels of HDL and increased carboxyhaemoglobin due to high carbon monoxide saturation which, leads to hypoxia in the arterial wall which ultimately end in atherosclerosis.[4]

10. Obesity:

Body mass index has a strong influence on the atherosclerotic process of the carotid arteries.[45] 20 % overweight is associated with increased risk.[44] In one study, body mass index is positively correlated with CIMT.[46]

EVALUATION OF CIMT BY DOPPLER ULTRASOUND-AN INDICATION OF ATHEROSCLEROSIS

High resolution B-mode ultrasound is a non-invasive technique widely used to assess atherosclerosis in superficial arteries. It allows the accurate measurement of the distance between blood–intima and media–adventitia interfaces of the carotid wall, which is defined as carotid intima-media thickness (IMT).[12] Several authors have suggested that carotid IMT is a marker of atherosclerosis in other vascular beds.[17]

Indeed, an increased carotid IMT has been associated with a number of atherosclerosis risk factors,[48,49] also associated with prevalence and extent of coronary artery disease (CAD)[18] and the incidence of new coronary and cerebral events.[17] In view of these relationships, carotid IMT has been proposed as a surrogate marker and used in clinical trials as an alternative to coronary atherosclerosis.[50]

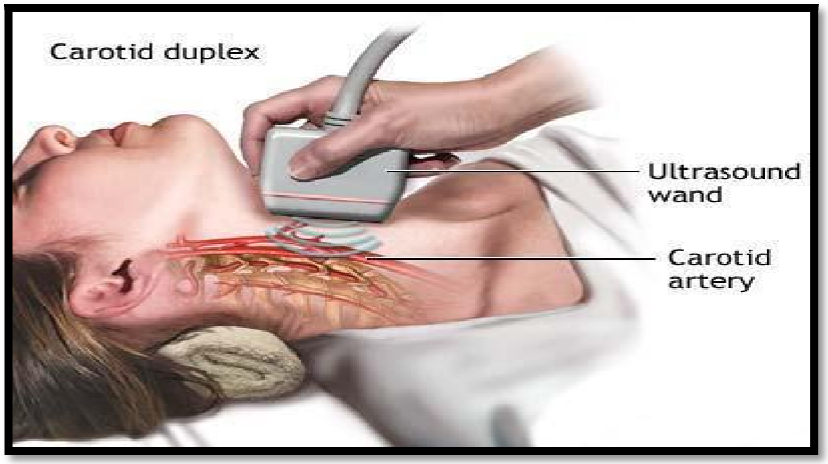


Figure-3: Sonographic evaluation of carotid arteries

Sonography of the Carotid arteries

B-mode imaging offers other advantages over angiography as it is non-invasive, risk free, and less expensive. It can also be used to assess progression or regression of atherosclerosis by multiple serial measurements. With all these advantages many investigators since mid 1980s have used B-mode ultrasonography as important tool to assess atherosclerosis in various clinical trials.[51,52]

Atherosclerosis is an inevitable accompaniment of ageing and its rate of development depends on several factors. Well known risk factors for accelerated atherosclerosis include hypertension, smoking, dyslipidemia and hyperglycemia. As several practical life style and pharmacological interventions for attenuating atherosclerosis development are available, it is necessary to find out peoples who are at early risk of developing accelerated atherosclerosis.

Measurement of intima-media thickness of extra cranial carotid arteries by B-mode ultrasound imaging well correlated with pathological examination. At present, The CIMT is a well studied ultra sonographic tool for early atherosclerosis. Although, the CIMT is a localized assessment,it can reflects the generalized atheroscelerotic changes in body.

The normal intimal + medial measurement of common carotid artery as evaluated by B mode ultrasonography imaging was approximately 0.80mm.[70] Few authors have approximated the CIMT with the formula as (0.009× Age+ 0.116).[71] CIMT is used in clinical trials as a surrogate marker for assessing the plaque and whether lipid lowering drugs decrease or reverse atherosclerosis.[53]

Carotid Arteries

There are two common carotid arteries placed on either side of the neck. Right common carotid artery is branch of brachio cephalic trunk (Innominate artery) which originates from arch of aorta at the level of right sterno clavicular joint .The left common carotid artery originates directly from the arch of aorta in between inominate vessel and left subclavian artery .

At the level of upper border of thyroid cartilage, the common carotid artery divides into external carotid artery and internal carotid artery.

At the beginning of internal carotid artery, there is a focal dilatation called as carotid sinus. The role of carotid sinus (bulb) is reflex hemodynamic modification due to the changes in the arterial blood pressure .It also acts as a

baro receptor for the control of intra cranial pressure. The chemoreceptor is seen behind the common carotid bifurcation, which looks like a reddish brown structure .

The carotid sheath contains carotid artery, internal juglar vein, vagus nerve. Within the carotid sheath, the artery medially placed and the vein is laterally placed and the nerve is posteriorly placed in between artery and vein.[47]

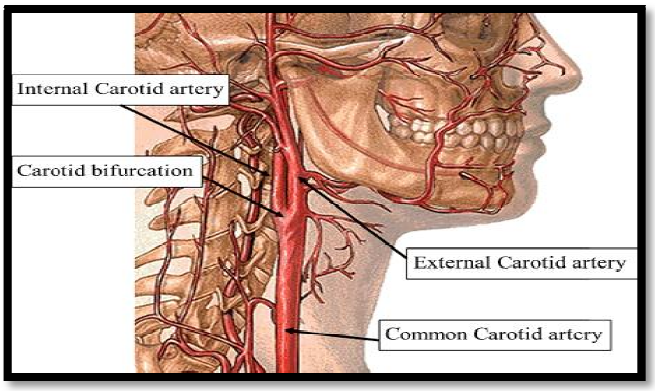


Figure-4: Lateral view of carotid arteries

External Carotid Artery

The external carotid artery forms at the level of third cervical disc and lateral to the upper border of thyroid cartilage. It ascends forward and divides into maxillary artery and superficial temporal artery at the the level of mandibular neck.

Internal Carotid Artery

At the begining of internal carotid artery there is a focal dilatation called as carotid bulb. Internal carotid artery ascends forward and entering into the

skull, through the carotid canal .Intracranially it divides into petrous, cerebral, cavernous and cervical branches. The Internal carotid artery supplies most of the cerebral hemisphere, nose, eye and forehead.

Diabetes Mellitus:

Definition[20]

Diabetes mellitus is defined as a group of metabolic disease, that are characterized by hyperglycemia ,altered fat and protein metabolism resulting from defects in insulin action, insulin secretion or both.

It is a syndrome comprising of neurologic, vascular and metabolic components. The chronic hyperglycemia of diabetes is associated with long term dysfunction of eyes, heart, kidneys, nerves and blood vessels

Classification of Diabetes mellitus

- Insulin dependent diabetes mellitus (IDDM)
    - Insulin receptor defect
    - Insulinopathies
    - Circulating anti receptor antibody
- Non- Insulin dependent diabetes mellitus (NIDDM)
- Other types of diabetes mellitus associated with specific conditions and syndromes like –
    - Hemochromatosis
    - Chronic or recurrent pancreatitis

- Pheochromocytoma
- Cushing's syndrome
- Glucagonoma
- Acromegaly
- Diuretics , beta blokers , glucocorticoids
- Lipotropic diabetes
- DIDMOAD syndrome
- Cystic fibrosis

- Malnutrition related diabetes mellitus
- Gestational diabetes mellitus

Epidemiology

The worldwide prevalence of Diabetes was calculated to be 2.8% in 2000 and estimated to increase upto 4.4% in 2030 including all age groups. The number of people with diabetes is calculated to increase from 171 million to 366 million 2030.This is because of mainly due to doubling of the urban population in developing countries between 2000 to 2030. The cause for increase in diabetes prevalence all over the world is mainly due to increase of the population aged more than 65 years.[21]

Prevalence of Diabetes in India

India leads the world with maximum number of diabetic patients term as "Capital of Diabetic World". The current prevalence of diabetic patients in India is calculated as 40.9 million and it is expected to be 69.9 million by 2025

Asian–Indian phenotype people have increased chance of developing diabetes and coronary artery disease due to certain unique clinical and biochemical alterations like greater abdominal adipocity (high Weight/ hip ratio, despite of low BMI) , increased insulin resistance ,higher level of high sensitive C – reactive protein ,low level of adiponectin ,lack of physical activity, high fat dietary pattern and increased urbanization . [23]

Figure-5: Diabetes prevalence in urban, semi urban and rural zones of India [24].

Diagnosis[21]

The National Diabetes Data Group and World Health Organization have issued diagnostic criteria for DM based on the following premises: (1) the spectrum of fasting plasma glucose (FPG) and the response to an oral glucose load (OGTT—oral glucose tolerance test) varies among normal individuals,

and (2) DM is defined as the level of glycemia at which diabetes-specific complications occur rather than on deviations from a population-based mean.

Criteria for the Diagnosis of Diabetes Mellitus[69]

- Symptoms of diabetes plus random blood glucose concentration ≥ 11.1 mmol/L (200 mg/dL)[a] *or*
- Fasting plasma glucose ≥ 7.0 mmol/L (126 mg/dL)[b] *or*
- Two-hour plasma glucose ≥ 11.1 mmol/L (200 mg/dL) during an oral glucose tolerance test[c]
- [a]Random is defined as without regard to time since the last meal.
- [b]Fasting is defined as no caloric intake for at least 8 h. [c]Venous plasma glucose 2–h after ingestion of 75g oral anhydrous glucose load If 2–h plasma glucose is not measured, status is uncertain as diabetes or IGT (Impaired Glucose Tolerance) cannot be excluded

Pathogenesis of type 2 diabetes mellitus[21]

The key events of development of diabetes include, abnormal insulin secretion, insulin resistance or both. The predominant defect noted in impaired glucose tolerance (IGT) is insulin resistance .Once the patient had inadequate insulin secretary functions, in addition to insulin resistance, they land up in overt diabetic state.

Genetic Considerations

- The genetic component has a major role in Type 2 Diabetes Mellitus compared to Type 1 Diabetes Mellitus. Type 2 Diabetes Mellitus concordance in identical twins falls between 70 to 90 %

- The offspring of type 2 diabetic patients, have an increased risk for getting diabetes. The risk approaches 40% if both mother and father was affected by type 2 DM.

- Many non diabetic first degree relative of type 2 diabetic patients shows insulin resistance as evidenced by reduction of skeletal muscle glucose uptake .

Insulin Biosynthesis, Secretion, and Action

Biosynthesis

- Pancreatic islet beta cells are responsible for the production of insulin. It is formed from Pre –pro insulin (single chain 86 amino acid precursor polypeptide). Pro-insulin formed from pre-pro insulin by removal of amino terminal signal peptide by proteolytic mechanism.

- Cleavage of internal 31- residue fragment from pro insulin produce ,C - Peptide and both chains of insulin (A chain , B chain) A chain composed of 21 amino acid and B chain composed of 30 amino acids, which are connected by disulphide bond.

- Both C- peptide and mature insulin are stored together in beta cell granule which is secreted simultaneously.

- C-peptide is useful marker of insulin secretion due to delayed clearance compared to insulin clearence and it also usful for evaluation of hypoglycemia, by discrimination of exogenous or endogenous source of insulin.

Secretion

The key regulator of insulin secretion in pancreatic beta cell is glucose. The other factors influencing insulin secretions from beta cells are gastrointestinal peptide, ketones, amino acids, neurotransmitters and various nutrients. The cut –off value for insulin secretion by glucose is more than 70 mg/dl. The glucose is transported into beta cells by GLUT-2 glucose receptors and it stimulates insulin synthesis by altering ion channels activity and enhancing protein translation and processing. The insulin secretogogue drugs act through the SUR – receptors.

The cause for maturity onset diabetes mellitus (MODY) is mutation of proteins involved in insulin secretion such as, SUR (sulfonylurea receptor); ATP, (adenosine triphosphate); ADP, (adenosine diphosphate), cAMP, (cyclic adenosine monophosphate). (Adapted from WL Lowe, in JL Jameson (ed): Principles of Molecular Medicine. Totowa, NJ, Humana, 1998.)

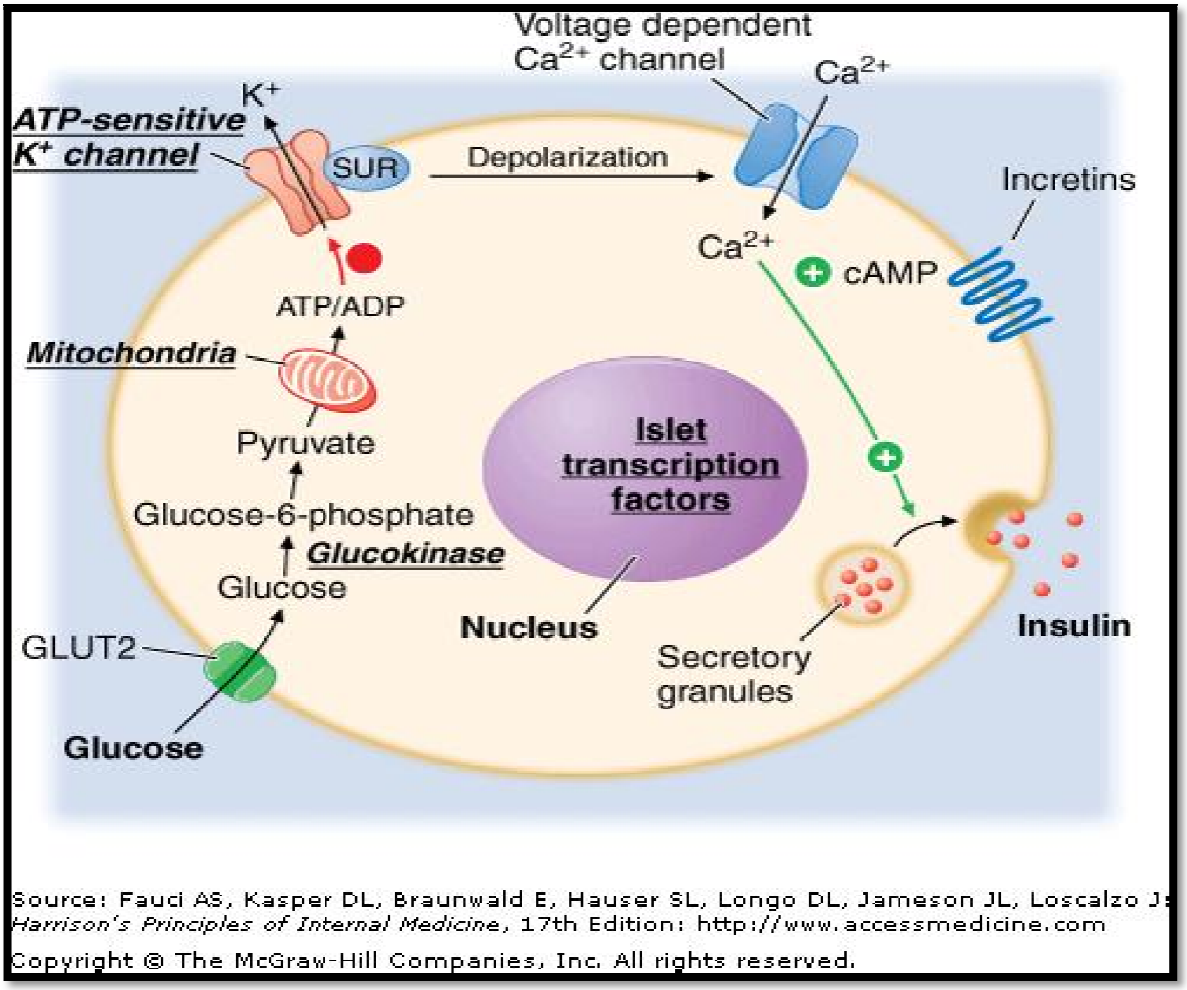


Figure-6: Diabetes and abnormalities in glucose-stimulated insulin secretion

ROLE OF DIABETES AND INSULIN IN ATHEROSCLEROSIS

Role of Insulin on Vascular Endothelium :

Insulin has both anti-atherogenic and atherogenic properties on vascular endothelium.

Table - 1 : Properties of Insulin

Anti-atherogenic	Atherogenic
Insulin stimulates the production of nitric oxide (Bi) From vascular endothelium which causes:	
• Vasodilatation.	• Vascular cell growth
• Prevents platelet aggregation.	• Synthesis of extracellular matrix
• Prevents growth of vascular smooth muscle cells (VSMC)	• Proteins and type IV collagen.
• Prevents migration an proliferation of VSMC.	• Modest effect on growth of VSMC and atherogenesis.
• Prevents formation of foam cells.	• Stimulation of growth factors.
• Inhibits expression of vascular adhesion molecular and secretion and intercellular adhesion molecule.	• Enhanced LDL receptor activity and cholesterol synthesis.

Anti-atherogenic action of insulin is predominant in normal individual with normal insulin sensitivity. Atherogenic action predominant in insulin resistance states.

Table – 2 : Mechanism of Insulin

Atherogenesis **Pathway-1**	**anti-atherogenesis:** **Pathway-2**
Insulin binds to receptor ↓ Intracellular protein 'shc' phosphorylated (docking protein) ↓ Couple with signaling proteins like mitogen activated protein kinase (MAP-K) ↓ Stimulates RAS, RAF, MEKK, MAPK (oncogenes) ↓ Extracellular matrix VSMC migration ↓ Atherogenesis	Insulin binds to insulin receptor ↓ Internationalization ↓ Insulin receptor protein 1 & 2 are phosphorylated (Docking proteins) ↓ Couple with signaling proteins like phosphatidylinositol-3 kinase) (Pl-3 kinase) ↓ Nitric oxide (NO) produced ↓ Anti-atherogenesis

The hyper pro-insulinaemia also produces increased amount of plasminogen activator inhibitor-1 in liver, which produce defects in fibrinolysis and favours towards vascular thrombosis.

Pathophysiology

The spectrum of components involved in type 2 DM is insulin resistance, impaired insulin secretion, abnormal fat metabolism, excessive hepatic glucose production and central obesity. Glucose tolerance are near

normal in the intial stage of diabetes despite insulin resistance, this is due to compensatory increase of insulin output by pancreatic beta cells. Due to disease progression such as progressive insulin resistance and compensatory hyper insulinemia, the beta cells are not able to sustain the hyper insulinemic state in certain individuals which leads to impaired glucose tolerance state (elevation of post prandial glucose). Due to diasease progression over a period of time, A further decrease of insulin secretion by altered beta cell function and increased hepatic glucose production leads to full blown diabetes (fasting hyperglycemia)

Metabolic abnormalities;

A. Abnormal Muscle and Fat Metabolism

B. Impaired Insulin Secretion

C. Increased Hepatic Glucose and Lipid Production

D. Insulin Resistance Syndromes

Chronic Complications of DM

The chronic complications of DM affect many organ systems and are responsible for the majority of morbidity and mortality associated with the disease.

Macrovascular complications

- Coronary artery disease
- Peripheral arterial disease
- Cerebrovascular disease

Microvascular disease

- Retinopathy
- Neuropathy
- Nephropathy

Mechanisms of Complications

Four prominent theories, which are not mutually exclusive, have been proposed to explain how hyperglycemia might lead to the chronic complications of DM.

- ❖ First theory is that increased intracellular glucose leads to the formation of advanced glycosylation end products (AGEs) via the nonenzymatic glycosylation of intra- and extracellular proteins.
- ❖ A second theory is based on the observation that hyperglycemia increases glucose metabolism via the sorbitol pathway.
- ❖ A third hypothesis proposes that hyperglycemia increases the formation of diacylglycerol leading to activation of protein kinase C (PKC).

- ❖ A fourth theory proposes that hyperglycemia increases the flux through the hexosamine pathway, which generates fructose-6-phosphate, a substrate for O-linked glycosylation and proteoglycan production.

CARDIOVASCULAR RISK FACTORS IN DIABETES MELLITUS[27]:

1) Hypertension
2) Abdominal obesity
3) Dyslipidemia
    a) Increased very-low-density lipoprotein- triglyceride
    b) Decreased high-density lipoprotein
    c) Small dense atherogenic low-density lipoprotein particles
    d) Postprandial lipemia
4) Elevated Plasminogen Activator Inhibitor-1 activity

Table – 3 : New risk factors and Mechanisms[28]

	Risk Factor	Mechanism
1.	Hyperglycemia	Glycation / oxidation of lipoproteins, vessel wall matrix / collagen. Increased diacylglyceral / PKC – altered growth factors, permeability and other vascular changes of arterial smooth muscle
2.	Hyperinsulinaemia / hyper-pro-insulinaemia /insulin resistance	Increases the plasminogen activator inhibitor 1 and increases small dense LDL.
3.	Dyslipidemia High TG Low serum HDL Small, dense LDL-C	Low serum HDL-C Atherogenesis Atherogenesis.
4.	Increased central obesity	Insulin resistance, dyslipidemia
5	Increased plasminogen – activator inhibitor- 1 (PAI-1)	Decreased fibronolysis.
6.	Increased platelet aggregation / adhesiveness	Increased thrombosis
7.	Increased fibrinogen concentration	Thrombogenesis, atherogenesis
8.	Increased plasma oxidative stress.	Endothelial damage, lipoprotein oxidation and atherogenesis

9.	Renal dysfunction	Atherogenesis, hypertension, oxidation
10.	Cardiovascular autonomic	Sudden death
11.	Abnormal vascular reactivity	Vasoconstriction, ischemia, hypertension
12.	Altered lipoprotein phenotype Increased lipo (a) Increased apo (B) LDL-phenotype B Decreased Apo AII	Atherogenesis
13.	Micro-albuminuria	Dyslipidemia, HTN

Chronic hyperglycemia and various coronary risk factors will increase the cardiovascular morbidity and mortality. For example, after controlling of all known cardiovascular risk factors, type 2 DM increases the cardiovascular death rate twofold in men and fourfold in women. Risk factors for macrovascular disease in diabetic individuals include hypertension, cigarette smoking, obesity, reduced physical activity, and dyslipidemia. The additional risk factors are more prevalent in the diabetic population include abnormal platelet function, macroalbuminuria, microalbuminuria and elevation of serum creatinine .

The insulin resistance, as evidenced by elevated serum insulin levels, is associated with an increased risk of cardiovascular complications in individuals with and without DM. Individuals with insulin resistance and type 2 DM have elevated levels of plasminogen activator inhibitors (especially PAI-1) and fibrinogen, which enhances the coagulation process and impairs fibrinolysis, thus, favoring the development of thrombosis. Diabetes is also associated with endothelial, vascular smooth-muscle, and platelet dysfunction.

MATERIAL AND METHODS

Source of data

The present study was carried out in patients with type 2 diabetes mellitus with and without coronary artery disease admitted in Coimbatore medical college hospital , Coimbatore . between the period of July 2014 to June 2015.

Methods of collection of data

Study design :

Cross sectional, case control study

Sample size:

Study group- 50 patients

Control group- 50 patients

Selection of patients:

The study group included 50 patients who are known cases of type 2 diabetes mellitus and presenting with acute coronary syndrome or with well documented history of established coronary artery disease.

The control group included 50 patients of type 2 diabetes mellitus without any history or evidence of coronary artery disease.

Inclusion criteria:

- Patients with type 2 diabetes mellitus of duration more than 2 years, with age more than 35 years , of either sex, receiving oral hypoglycemic agents or insulin or both.

- Patients with evidence of acute coronary syndrome or old ischemic heart disease (applicable only for study group).

Exclusion criteria:

- Patients with chronic renal disease

- Patients with thyroid disease

- Patients with hepatic disease

- Patients with history of stroke

- Patients with rheumatoid disease

Study protocol:

All patients included in the study group underwent detailed clinical history analysis, physical examination and necessary investigations.

DEFINITIONS:

Pt is said to be diabetic – if:

They are known diabetics with definite history of treatment with OHA/ insulin.

Coronary Artery Disease is defined in the presence of minimum 2 of following[26].

1. Chest pain suggestive of Cardiac Origin.

   [Retrosternal squeezing. Radiating, increases with exertion, not relieved by rest and relieved by nitrates and associated with sweating.]

2. Creatine kinase – MB (CPK MB), at least four times, the upper limit of lab range or qualitatively positive TROP – I assay.

3. Electrocardiographic changes. This consists of ≥1 of the following.

   - ST segment elevation of ≥2mm (0.08 Sec.) From J Point in 2 related electric fields with typical evolutionary changes.
   - Presence of new pathologic Q waves in 2 related electric fields. [for Q-M.I.]

Non Q-wave M.I. are included in our study with ST depression and T inversion plus elevation in cardiac enzymes and typical chest pain. Also this study included patients with previous documented history of coronary artery disease.

Blood pressure was categorized according to following criteria.

Table – 4 : Classification of Blood Pressure for adults [25]

BP Classification	SBP mm Hg	DBP mm Hg
Normal	<120	<80
Prehypertension	120-139	80-89
Stage 1 hypertension	140-159	90-99
Stage 2 hypertension	≥160	≥100

Patients are said to be smoker if he smokes regularly≥5 beedies/ cigarettes per day.

Body-mass-index (Quetelet index) [67]

It is a measure of nutritional status of person.

It is calculated as follows.

BMI = Weight (in Kgs) / Height^2(in metres)

expressed as Kg/m^2

Table – 5 : BMI classification

Category	BMI (kg/m^2)	
	Males	**Females**
Under nourished	<20	<18
Normal	20 – 25	18 – 23
Over weight	25 – 27	23 – 25
Obese	> 27	> 25

Waist-hip (W:H) ratio:

It is a measure of central obesity. Waist is measured at umbilicus or midway between iliac crest and costal cartilage and expressed in cms. Hip is measured at iliac crest and expressed in cms. Then waist is divided by hip and W: H ratio is calculated

For females,

0.71 to 0.85 (Normal), > 0.85 (High)

For males,

0.85 to 0.89 (Normal), > 0.9 (High)

High W:H ratio indicates central or visceral adiposity [Apple shape body]. It is directly related as risk factor for certain diseases like diabetes (type–2). dyslipidaemia and CAD disease and is more relevant in Indian Setting.

Dyslipidaemia:

While quantifying lipid levels National Cholesterol Education programme (NCEP) – ATP III [68], (revised in 2002) criteria is followed.

Table- 5 : Dyslipidaemia classification

Risk	LDL Cholesterol	HDL Cholesterol	Triglycerides	Total Cholesterol
Higher	≥130	<35	≥400	≥240
Borderline	100 – 129	35 – 45	200 – 399	200 – 239
Lower	< 100	> 45	<200	<200

Biochemical parameters:

HbA_1C: Done by ion exchange resin

Lipid profile:

After overnight fasting of 12 hours blood collected in the morning about 5 ml and the serum centrifuged and kept for analysis.

Serum cholesterol estimation: The CHOD-PAP method, enzymatic colorimetric test was used.

Test principle:

Table- 7 Test principle of cholesterol estimation

1.	Cholesterol ester + H_2O + RCOOH	Esterase »	Cholesterol
2.	Cholesterol + O_2	⟶ Oxidase	A^4 Cholesterol + H_2O_2
3.	$2H_2O_2$ + 4 amino phenazone + phenol	⟶	4p-benzoquinone – mono amino phenazone

Measured by colourimeter

Serum HDL Cholesterol (Phosphotungustate precipitation method):

Chylomicron, VLDL and LDL are precipitated using phosphor tungstic acid and Mg ions to serum sample. The supernatant contains only HDL detected using CHOD-PAP method.

Serum Triglyceride Estimation: Serum triglyceride estimation is done using GPO-PAP method which is an enzymatic colorimetric test.

Serum LDL Estimation: Serum LDL is calculated using Frield-Walds formula.LDL cholesterol = Total cholesterol – (HDL + Tg/5)

Routine tests for infection like DC, TLC, urine, chest X-ray, ESR were carried out.

Serum Urea: Serum urea is measured using urease method.

Serum Creatinine: It is measured using alkaline pictrate method.

Carotid imaging

The high frequency (≥ 7MHZ) linear probe is used for measuring carotid intima media thickness. It can be assessed by B mode ultra sonography or Doppler ultra sonography. The arteries visualized in the neck is

1. Common carotid artery
2. Bifurcation of common carotid artery
3. Extracranial part of internal carotid artery
4. External carotid artery

The common views used in carotid imaging is

A. Long axis view
B. Short axis view

Real time recording of these images allows study of pulsation patterns and movement of intimal flaps or complex plaques. The postero lateral approach usually is optimal for measurements of plaque formation and residual lumen, because plaques most often occur on the posterior wall of the carotid arteries. B-mode imaging is most accurate when the sound beam is perpendicular to the interface being imaged.

Carotid arteries are examined bilaterally in the areas of common carotid artery

The carotid arteries scanned by high resolution B-mode or colour Doppler Ultra sonography by using high frequency linear probe. The commonly used carotid arteries are common carotid artery and extra cranial part of internal carotid artery

The images shows two echogenic lines in the carotid artery. The inner echogenic lines represent the intimal interface and outer echogenic lines represent the collagen containing upper tunica adventitia

In longitutinal view, three IMT measurements was taken in the carotid artery. First measurements was taken from the site of greatest thickness and other two measurements was taken from 1cm above and 1 cm below from the first measurement. This three values are then averaged.[51,52] Measurement of the intima-media thickness, which increases in the early stages of plaque formation, is used as a surrogate marker for clinical trials assessing whether lipid lowering medications might slow or reverse atherosclerosis.[53]

Statistics:

The data obtained from the above was filled in the master chart and analysed further for their statistical significance. Data were presented as mean±SD values were called significant (if $p<0.05$). The correlation coefficient test and student t-test was used in most cases to compare frequency distribution.

RESULTS

In the present study, a total of 50 type 2 diabetic cases with coronary artery disease admitted as in-patients under the department of Medicine, Coimbatore medical college hospital, Coimbatore during the period of July 2014 to June 2015 were included. A total of 50 diabetics without evidence of coronary artery disease were taken as control.

Table-8 Age and Sex distribution of study group

Age	**M**	**%**	**F**	**%**	**Total**	**%**	**CIMT Mean± S.D.**
35-44	2	6.67	1	5.0	3	6.0	1.05±0.17
45-54	4	13.30	5	25.0	9	18.0	1.14±0.28
55-64	9	30.03	8	40.0	17	34.0	1.24±0.34
65-74	13	43.33	5	25.0	18	36.0	1.26±0.22
>75	2	6.67	1	5.0	3	6.0	1.28±0.16
Total	30	100%	20	100%	50	100%	
CIMT Mean±S.D.	30	1.24±0.20	20	1.19±0.40	50	1.197±0.35	

In the study group there are totally 50 patients, of whom 30 are male and 20 are female patients. Maximum numbers of patients in study group are fall in 65 to 74 years of age, in both male and female. Mean age in study group is 61.44±11.26. The mean CIMT in males is 1.22±0.35 and in females, it is 1.19±0.36 and is statistically not significant ('t'=0.68, p>0.05).Comparing age with CIMT in study group correlation coefficient 'r'=0.95, p<0.05 statistically significant.

Figure-7: Comparing male and female in study group with respect to age

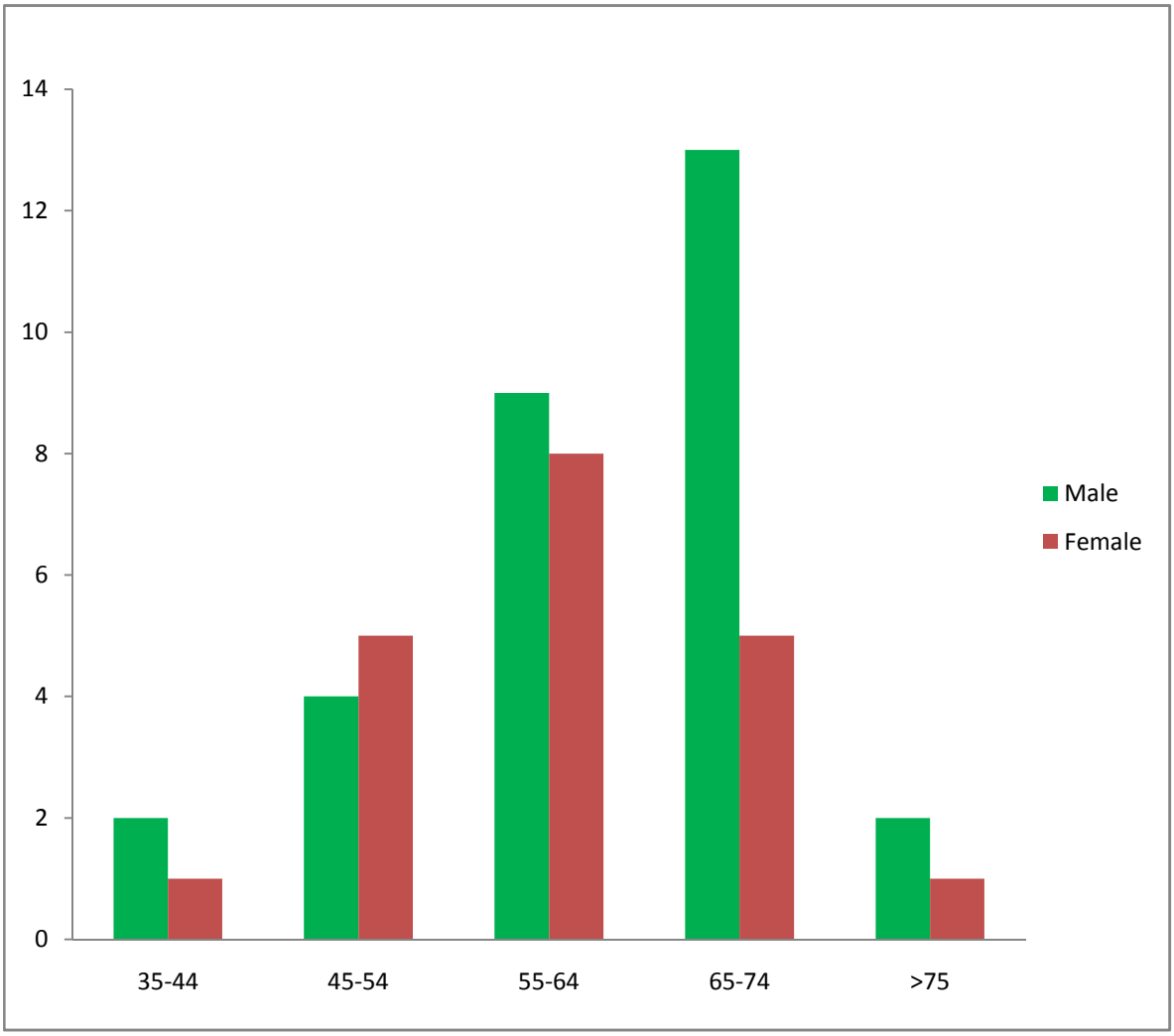
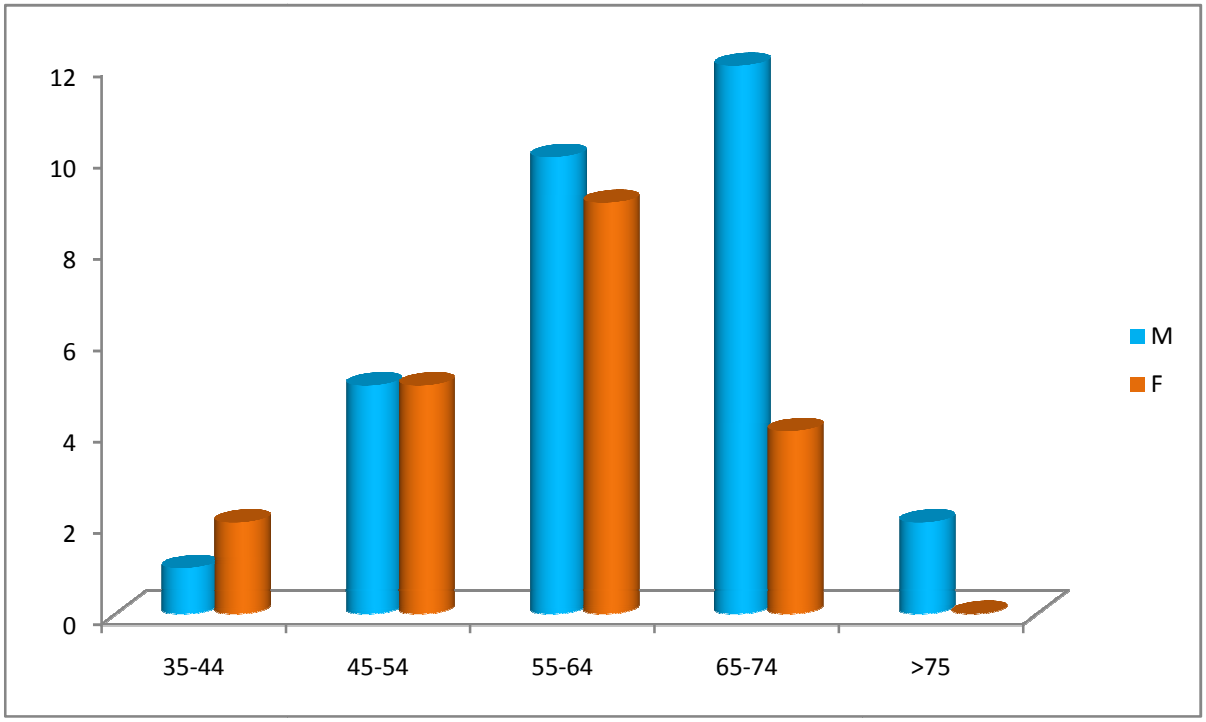


Table-9 Age and Sex distribution of control group

AGE	M	%	F	%	Total	%	CIMT Mean ±S.D.
35-44	1	3.33	2	10.00	3	6.00	0.87± 0.07
45-54	5	16.66	5	25.00	10	20.00	0.98± 0.33
55-64	10	33.33	9	45.00	19	38.00	1.01± 0.27
65-74	12	40.00	4	20.00	16	32.00	1.06 ± 0.08
>75	2	6.66	0	-	2	4.00	1.12 ± 0.13
Total	30	100%	20	100%	50	100%	
CIMT Mean ± S.D.	30	0.98± 0.28	20	0.96	50	0.97± 0.30	

In the control group, a total of 50 patients are taken of which, 30 male patients and 20 female patients. In male patients they were observed more to be in 65-74 yrs . whereas, in female patients, they were observed more to be in 55 to 64 yrs. The mean age of control group is 58.37±7.95, whose association is statistically not significant ('t'=0.23, p>0.05). The mean carotid IMT of males in control group is 0.98±0.28 as against 0.96 in female patients. Mean CIMT of control group is 0.97±0.30. On comparing age with CIMT in control group, correlation coefficient 'r'=0.93, p<0.05 statistically significant.

Figure- 8: Comparing male and female in control group with respect to age



Comparing age between study and control group student 't'= 1.52 and p>0.05 which is not significant. On comparing sex among both groups, there is no statistical significance(Chi square test $X^2 = 0.73$, p>0.05).

Table- 10 Comparison of CIMT between study and control groups

Study group CIMT Mean± S.D.	Control group CIMT Mean± S.D.	t-test	p value
1.197± 0.35	0.97± 0.30	t = 3.23	p<0.01 (highly significant)

The mean CIMT in study group is 1.197±0.35. Whereas, mean CIMT in control group is 0.97±0.30. On comparison of both groups, it shows statistical significance ('t'=3.23, p<0.01).

Table-11 Predominant Symptom presentation of study group

Symptoms	Number of cases	Percentage
Chest Pain	30	60
Shortness of Breath	10	20
Sweating	10	20
Palpitations	-	-
Syncope	-	-

In the study group out of 50 patients, the predominant symptom was chest pain (60%). But many patients presented with multiple symptoms. Though, only main chief complaint is taken into account in this table.

Table-12 Duration of Diabetes mellitus and CIMT

Study						Control		
Duration	**No**		**%**	**CIMT.**		**No.**	**%**	**CIMT**
<5 years	20		40.00	1.15± 0.35		22	44.00	0.84 ± 0.19
6- 10 yrs	25		50.00	1.18±	0.30	23	46.00	1.04 ± 0.35
11-15 yrs	4		8.00	1.24±	0.08	3	6.00	1.24 ± 0.24
16-20 yrs	1		2.00	1.31±	0.13	2	4.00	1.26 ± 0.26
	50		100	1.21± 0.30		50	100	0.98 ± 0.27

As the duration of diabetes mellitus increases the mean CIMT also increases, which is very much evident from the data. The mean duration of diabetes in both study and control groups is 6.65± 3.75 and 7.18± 2.78 respectively, which is statistically not significant (student 't'=0.93, p>0.05). On comparing both duration of diabetes with progression of CIMT in both study and control groups, the correlation coefficient 'r'=0.823, and 'r' = 0.825 respectively, Which is statistically highly significant (p<0.01)

Figure-9 comparison of Duration of Diabetes mellitus with CIMT

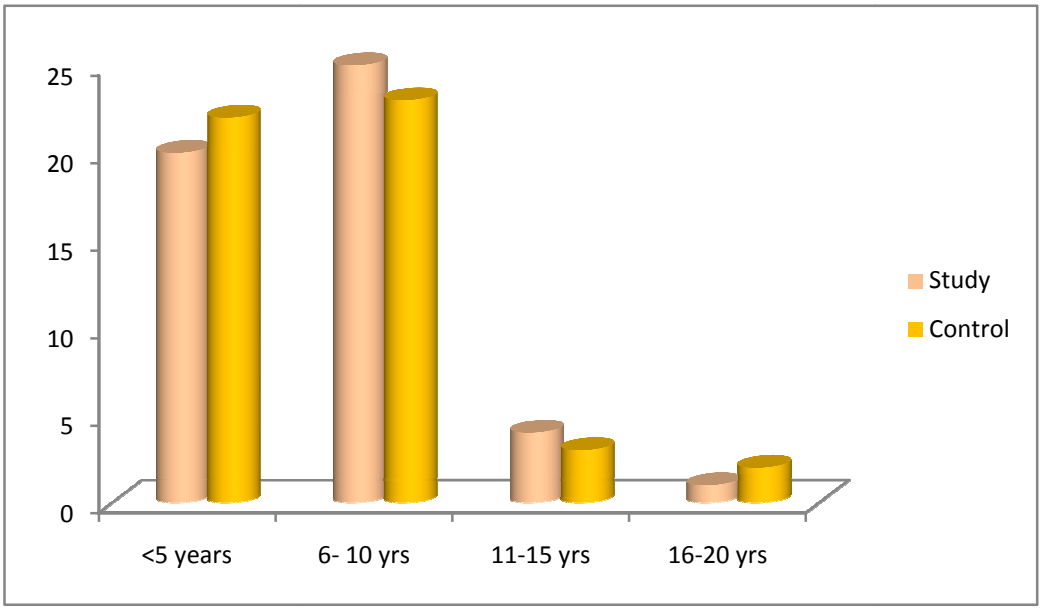


Table-13 Relation of Smokers and CIMT

	Study			Control		
Smoker	No	%	CIMT Mean ± SD	No	%	CIMT Mean ± SD
Yes	20	40	1.37±0.27	17	34.00	1.14±0.23
No	30	60	1.08±0.32	33	66.00	0.93±0.33
Total	50	100	1.197±0.33	50	100	0.976±0.30

In the present study 40% of study group are smokers with mean CIMT (1.37±0.27), which is much higher than non smokers (mean CIMT 1.08±0.32) and smokers of control group (mean CIMT 1.14±0.23). Smokers have higher CIMT compared to non smokers in both groups which is statistically significant ($p<0.05$). On comparison of smoking with CIMT, Student 't'=3.35 in study group and 't'=2.07 in control group.

Figure-10: Number of Smokers in both groups

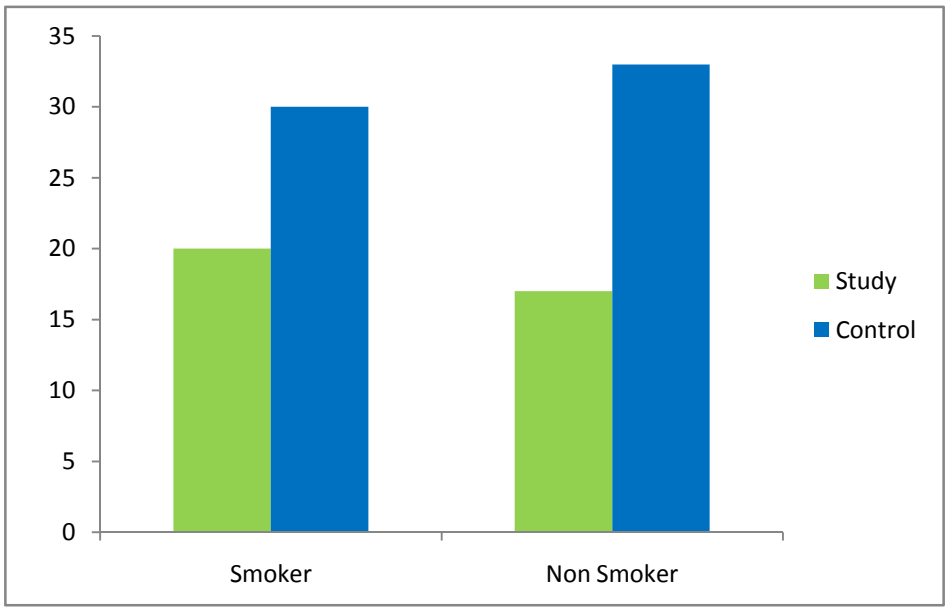


Table-14 Number of patients on various therapies of diabetes

Treatment	Study group	%	Control group	%
Insulin	8	16.00	10	20.00
OHA	37	74.00	35	70.00
Both	3	6.00	4	8.00
None	2	4.00	1	2.00
Total	**50**	**100**	**50**	100

A very high number of patients in both study and control group were on OHA's (68% & 70% respectively). Only 2 patients in study group and 1 patient in control group were not on any treatment. There is no statistical significance found between patients on Insulin or OHA's or both (p>0.05 Not Significant).

Figure- 11: Various therapies of diabetes in both groups

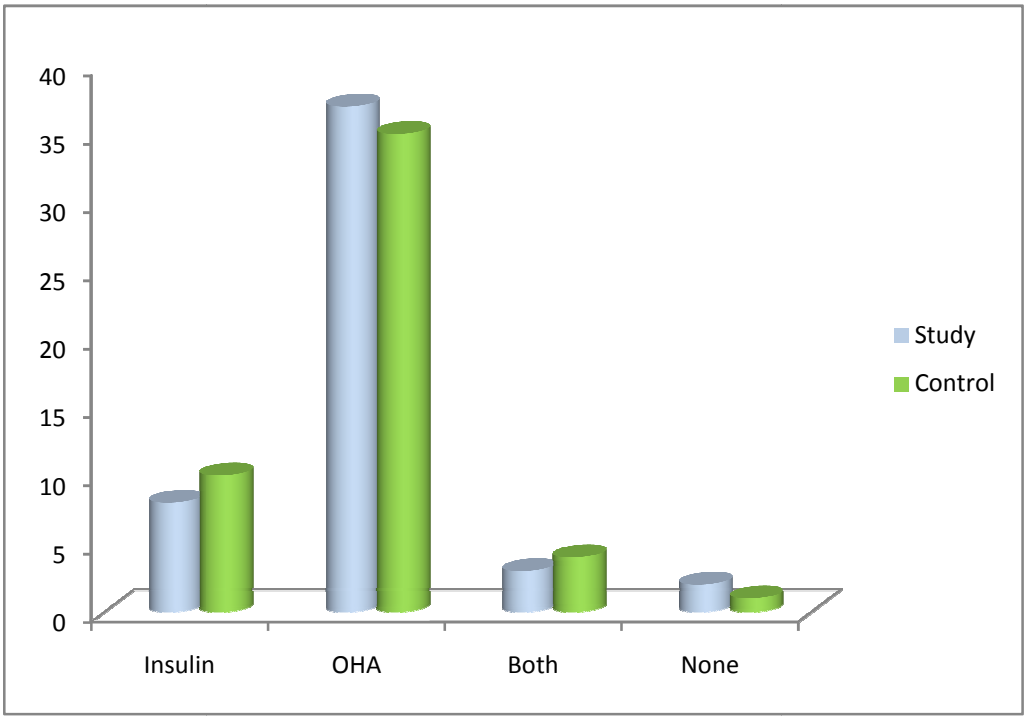


Table-15 BMI in study and control group

BMI	Study group	%	Control group	%
< 18.5	3	6.00	4	8.00
18.5-24.9	24	48.00	30	60.00
25-29.9	20	40.00	15	30.00
>30	3	6.00	1	2.00
Total	**50**	**100**	**50**	**100**

In the present study, the mean BMI in study and control group were 25.42±4.74 and 23.19±4.79 respectively, which was highly significant ('t'=2.68, p<0.01). There is no statistical significance noted on comparing changes of BMI with CIMT in both study and control groups (p>0.05 in both groups).

Figure- 12: Comparison of BMI with both groups

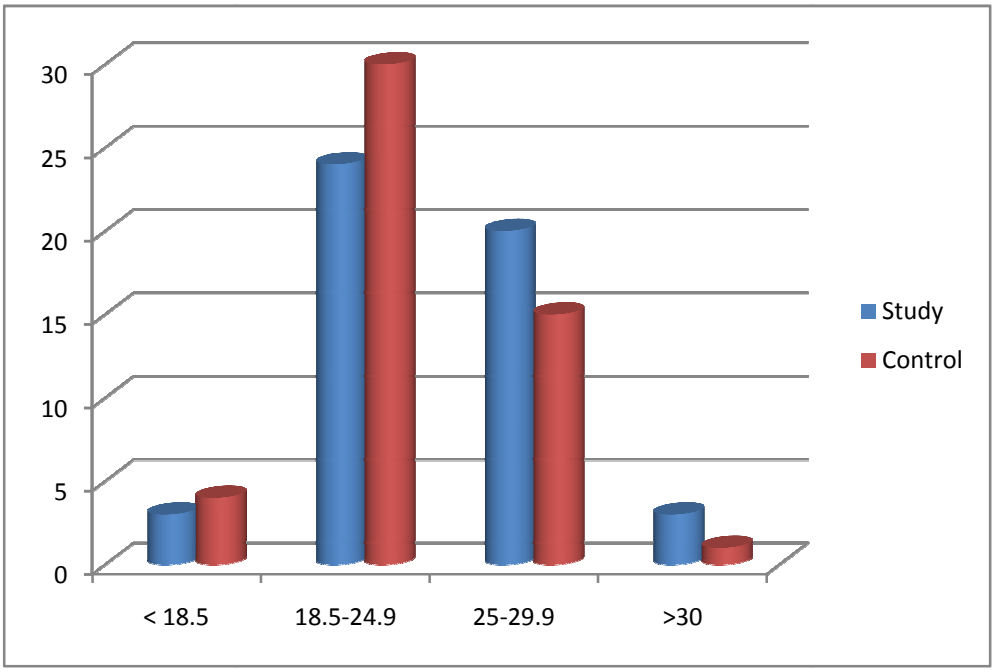


Table-16

Waist Hip Ratio in study and control group

W/ H/ Ratio	Study group	%	Control group	%
Male ≤ 0.9	4	8.00	6	12.00
> 0.9	26	52.00	24	48.00
Female ≤ 0.85	5	10.00	7	14.00
> 0.85	15	30.00	13	26.00
Total	**50**	**100**	**50**	**100**

In the present study, The mean waist hip ratio of study and control groups is 0.949±0.112 and 0.95±0.044 ($p>0.05$, not significant). There is no statistical significance found between increase in waist hip ratio with CIMT ($p>0.05$ in both groups).

Figure- 13: Comparison of Waist Hip Ratio in study group

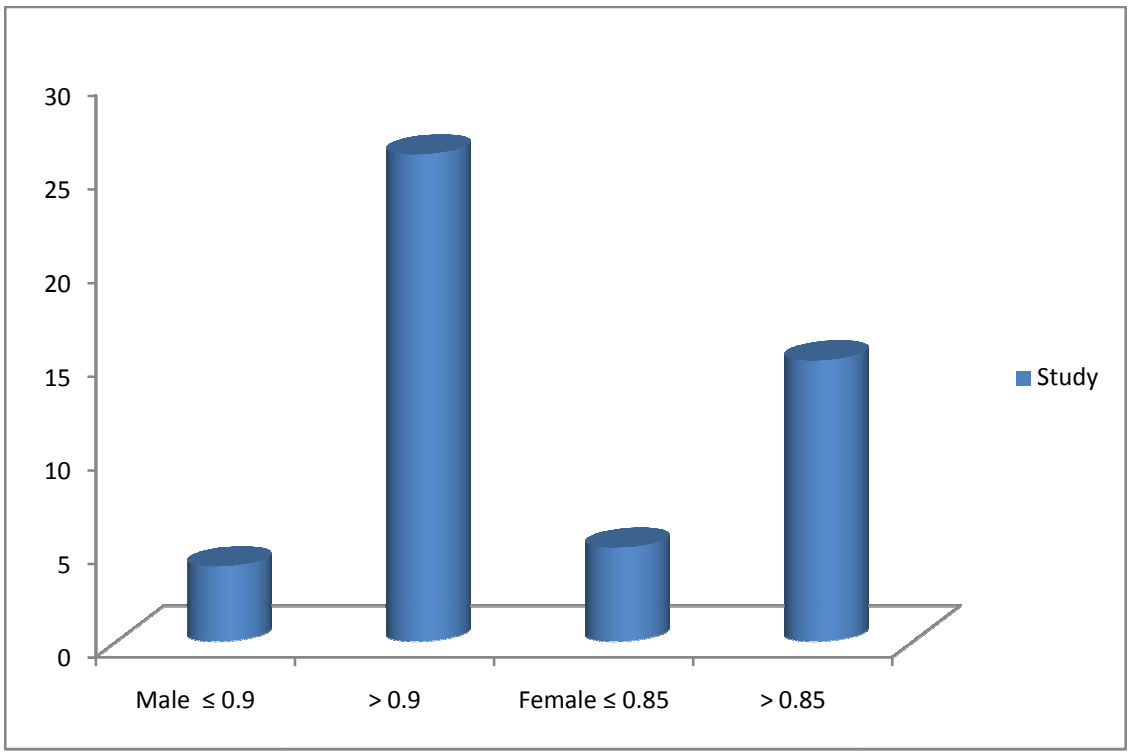


Figure- 14: Comparison of Waist Hip Ratio in control group

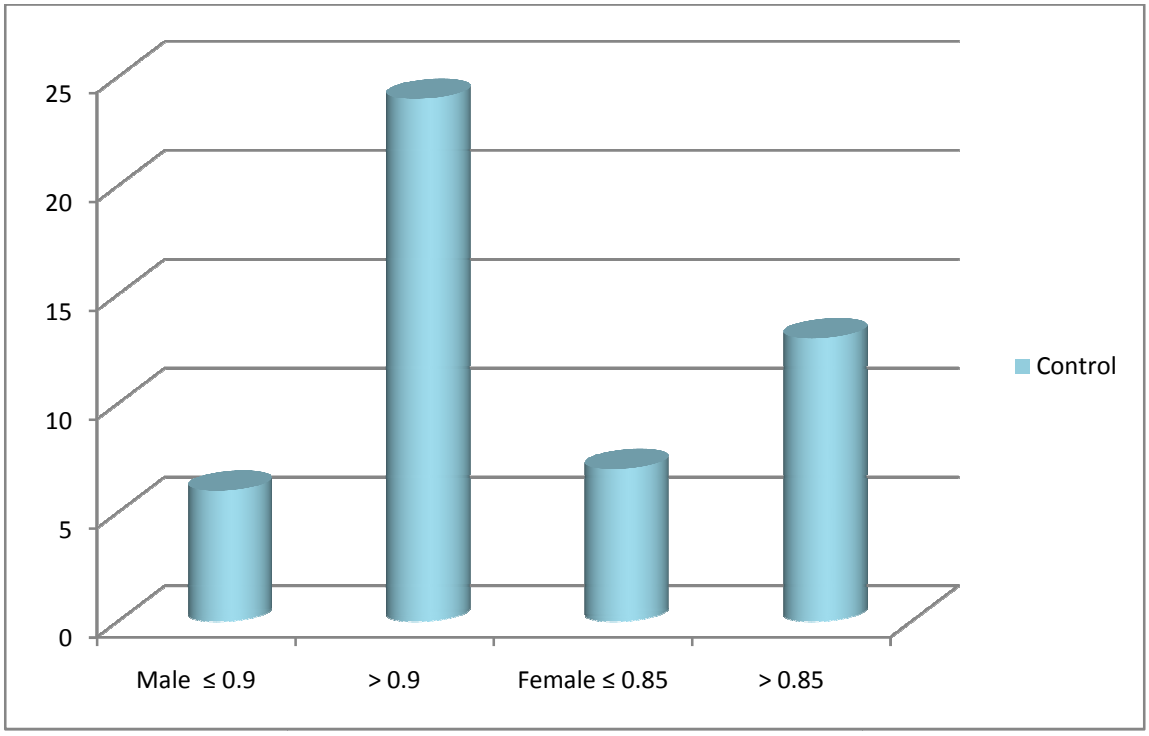


Table-17 SBP in study group and control group

SBP	Study	%	Control	%
≤ 139	12	24.00	30	60.00
140-160	19	38.00	15	30.00
>160	19	38.00	5	10.00
Total	**50**	**100%**	**50**	**100%**

In the study group, The mean SBP is 154.48±22.6 and in control group mean SBP is 133.33±14.4. On comparing SBP between both groups coefficient correlation is 4.8 and is statistically very highly significant ($p<0.001$). On comparing SBP with changes in CIMT is statistically significant in both groups ($p<0.01$).

Figure-15 comparison of SBP in study group and control group

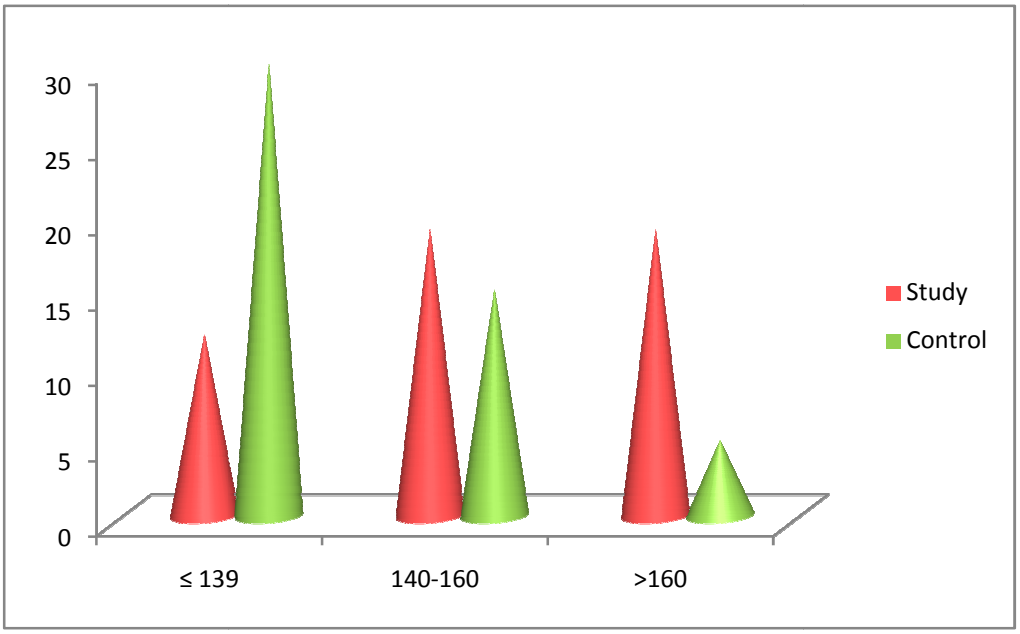


Table-18 DBP in study and control group

DBP	Study	%	Control	%
≤ 80	12	24%	25	50%
81-90	23	46%	18	36%
>90	15	30%	7	14%
Total	**50**	**100%**	**50**	100%

Mean DBP in study and control groups is 90.8± 10.14 and 84.27± 7.37 respectively, which on comparison is statistically very highly significant (correlation coefficient 'r'=3.18, p<0.001). On comparing DBP with progression of CIMT is statistically significant in both groups (p<0.01)

Figure-16 comparison of DBP in study group and control group

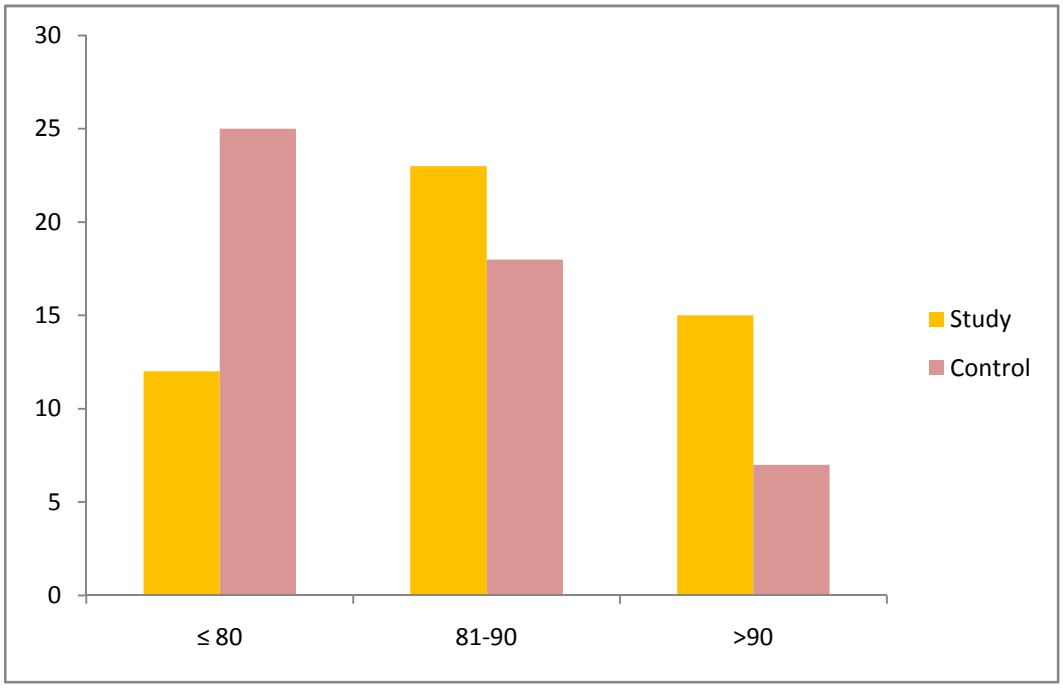


Table-19 HbA_1C in study and control group

HbA_1C	Study group	%	Control group	%
≤ 7	5	10	8	16
>7	45	90	42	84
Total	**50**	**100**	**50**	**100**

In the present study, correlation between HbA1C in study and control groups is statistically not significant. Also correlation of CIMT with HbA1C in study group is not significant ($p>0.05$). Whereas, it is significant in control group ($p<0.05$).

Figure- 17 Comparison of HbA_1C in study and control group

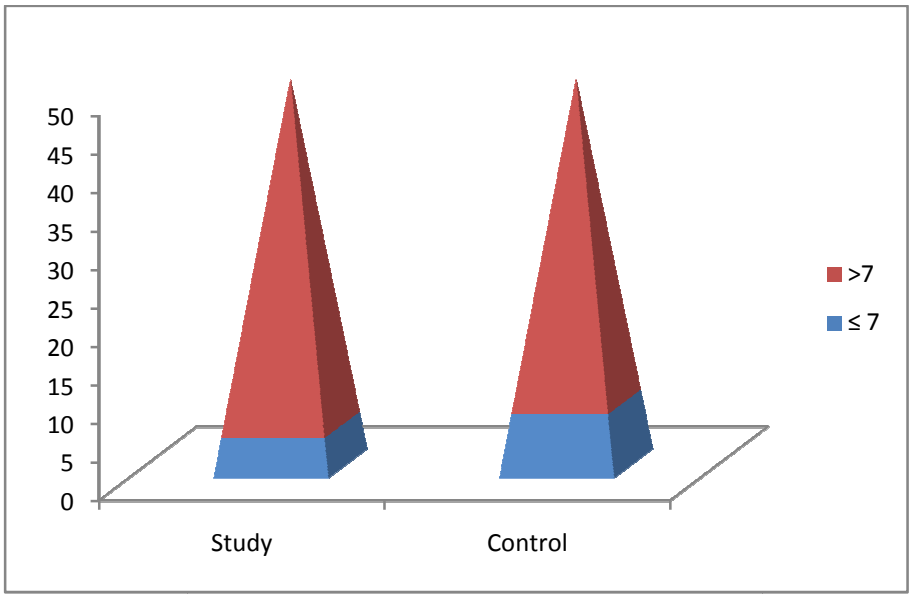


Table-20 Total Cholesterol in study and control group

Total-C	Study group	Control group
< 200	25	30
200-240	15	15
>240	10	5
Total	**50**	**50**

In the present study, mean total cholesterol in study and control groups was found to be 193.97±38.74 and 169.1±47.56 respectively. (t=2.55, p<0.01 highly significant). On comparison of total cholesterol with CIMT in study group showed statistically positive correlation (correlation coefficient 'r'=0.604, p<0.01). the control group also showed significant positive correlation between total cholesterol and CIMT (correlation coefficient 'r'=0.665, p<0.01).

Figure-18 : Comparison of Total Cholesterol in study and control group

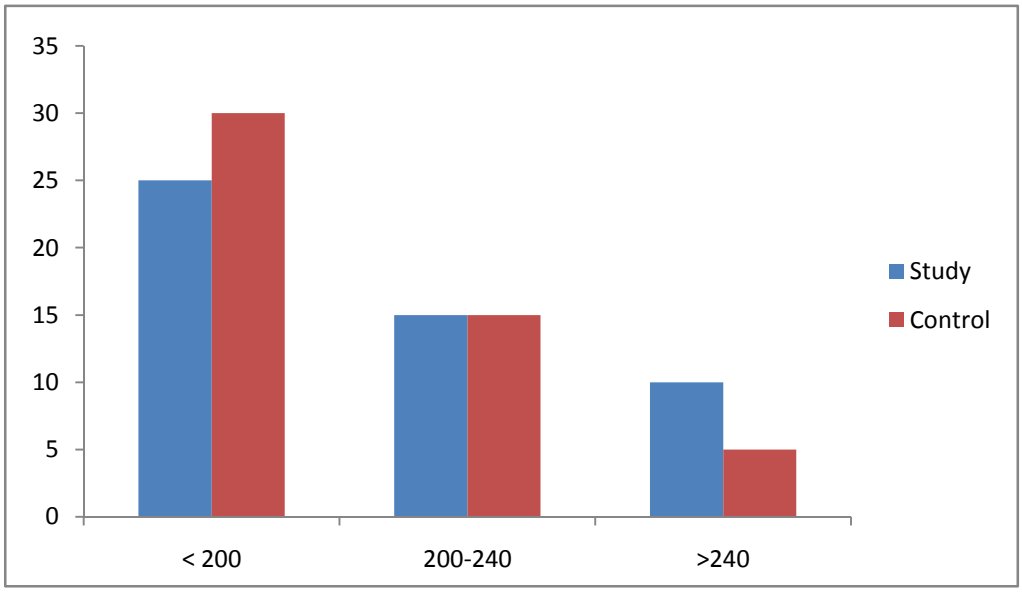


Table-21 HDL-Cholesterol in study and control group

HDL-C	Study group	Control group
Male ≤ 40	20	18
> 40	10	12
Female ≤ 50	19	18
> 50	1	2
Total	**50**	**50**

The mean HDL cholesterol in study and control groups were 39.644± 2.84 and 38.8± 5.85, which was not significant (p>0.05). The study group and control group showed progression of CIMT had negative correlation with HDL-C (correlation coefficient 'r'= -0.679, p<0.01 and 'r' = -0.668, p<0.01 respectively), which is statistically significant.

Figure-19 Comparison of HDL-Cholesterol in study and control group

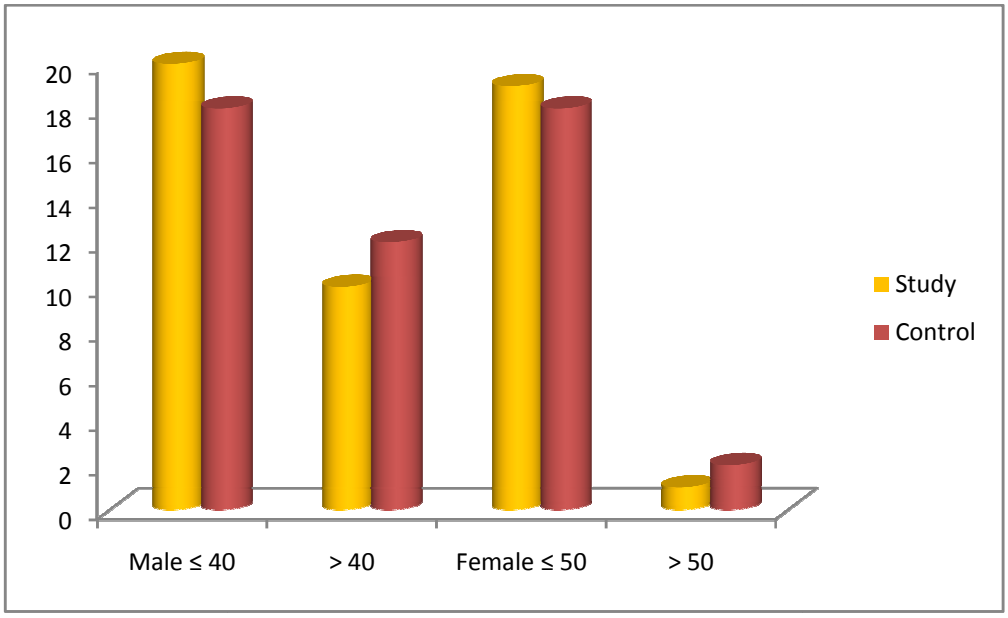


Table-22 LDL Cholesterol in study and control group

LDL-C	Study group	Control group
< 100	16	28
101-130	14	15
131-159	7	4
160-199	13	2
>200	0	1
Total	**50**	**50**

The present study group, which showed significant positive correlation ($p<0.01$) between LDL-C and CIMT. It is very much comparable to above studies. The mean LDL-C in study and control groups is 138.904± 36.11 and 121.166± 49.98 respectively, which is statistically significant ($p<0.05$).

Figure-20: Comparison of LDL Cholesterol in study and control group

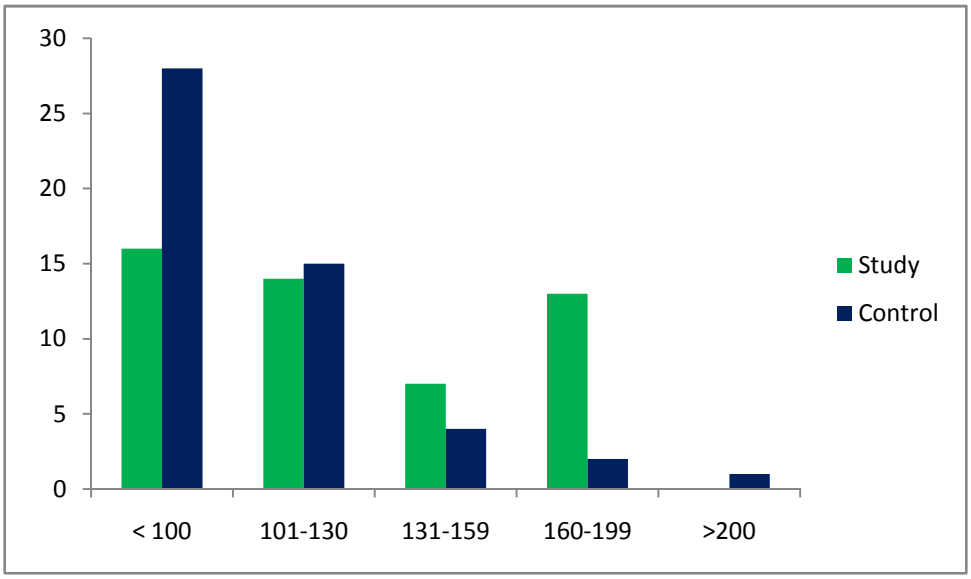


Table-23 Triglycerides in study and control group

TG	Study group	Control group
<150	16	25
151-199	20	20
200-499	14	5
>500	0	0
Total	**50**	**50**

In the present study group a positive correlation is found between triglycerides and progression of CIMT (correlation coefficient 'r'=0.839), which is statistically significant ($p<0.01$). The values in control group were very much similar to study group (correlation coefficient 'r'=0.688, $p<0.01$ statistically significant). The mean values of triglycerides in study and control group were 199.86± 63.1 and 140.46± 52.1 respectively, which is statistically very highly significant ($p<0.001$).

Figure- 21 Comparison of Triglycerides in study and control group

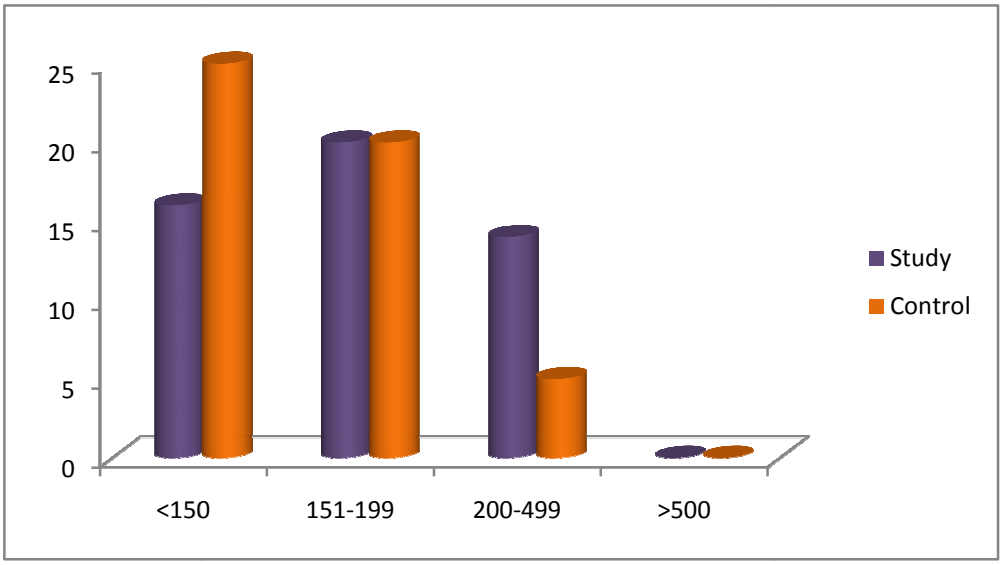


Table-24 Sr.creatinine in study and control group

Sr.creatinine	Study group	Control group
<1	15	25
1-1.2	18	15
>1.2	17	5

Mean Sr. creatinine in study and control group is 1.24 ± 0.41 and 0.98 ± 0.27 respectively. On comparison, which is statistically very highly significant (t-test 3.25, p<0.001). On comparing , Sr.creatinine with progression of CIMT is not statistically significant in both groups.

Figure- 22 Comparison of Sr.Creatinine in study and control group

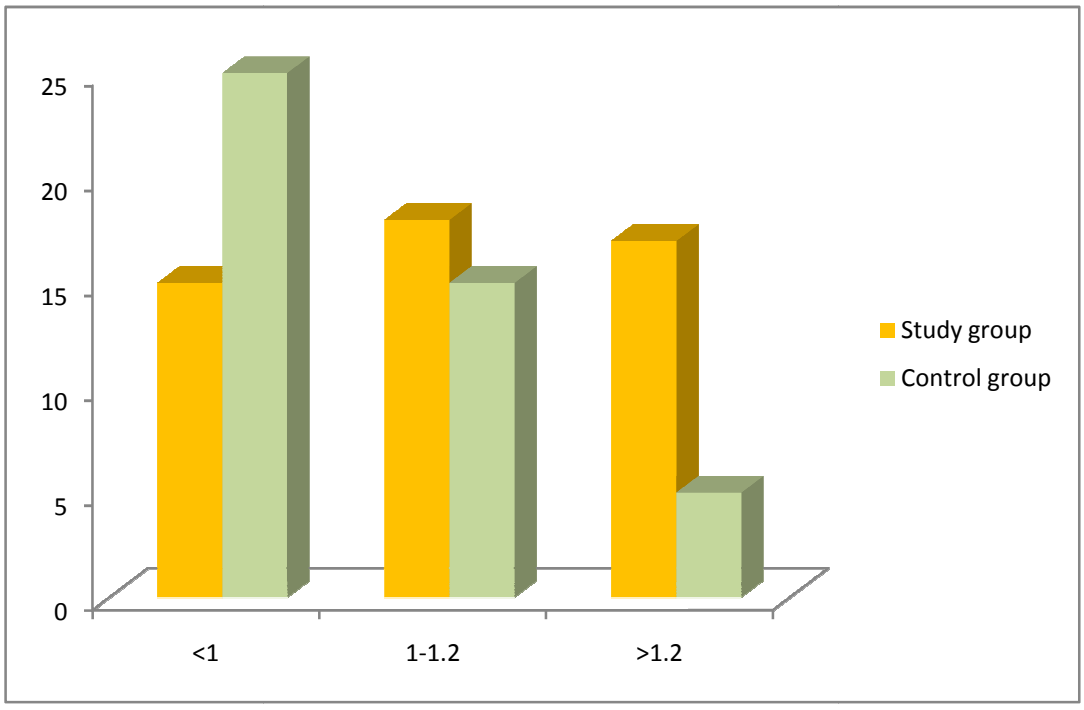


Table-25 FBS in study and control group

FBS	STUDY	CONTROL
≤ 130	15	40
131 - 179	28	10
≥ 180	7	0

Mean FBS in study and control group is 155.7 ± 56.2 and 125.34 ± 14.9 respectively. On comparison, which is statistically very highly significant (t-test 3.68, $p<0.001$). On comparing, FBS with progression of CIMT is not statistically significant in both groups.

Figure- 23 Comparison of FBS in study and control group

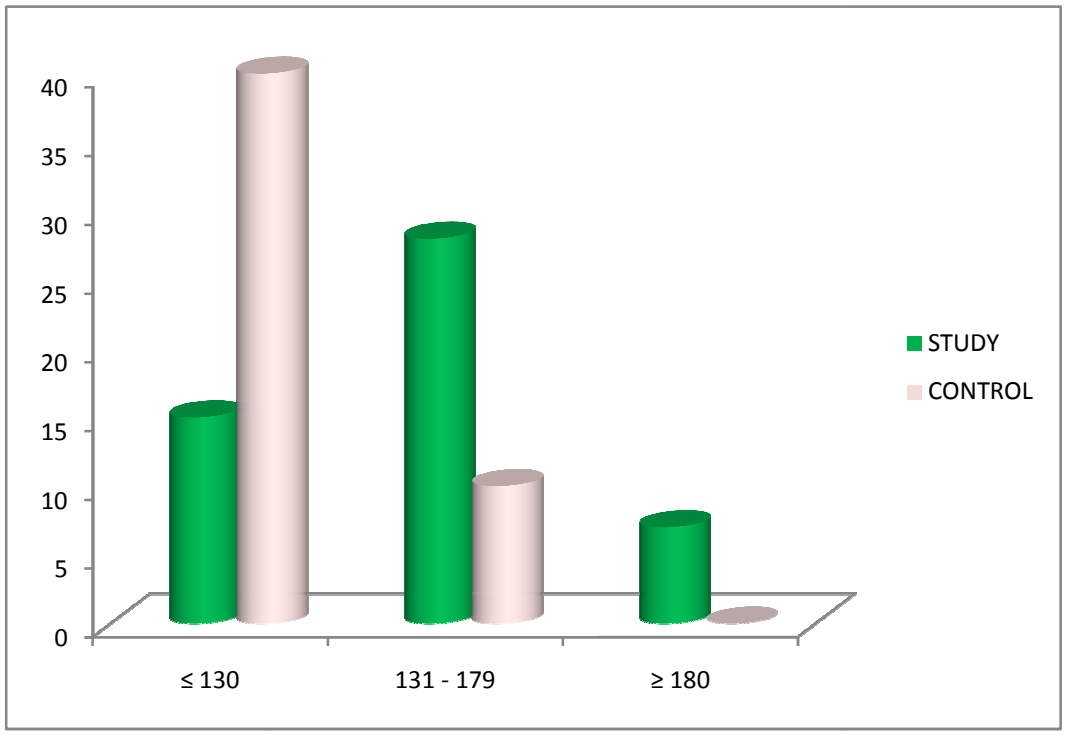


Table-26 PPBS in study and control group

PPBS	study	control
≤ 150	2	7
151 -199	28	35
≥ 200	20	8

Mean PPBS in study and control group is 217.2 ± 74.01 and 168.44 ± 23.45 respectively. On comparison, which is statistically very highly significant (t-test 4.36, p<0.001). On comparing, PPBS with progression of CIMT is not statistically significant in both groups.

Figure- 24 Comparison of PPBS in study and control group

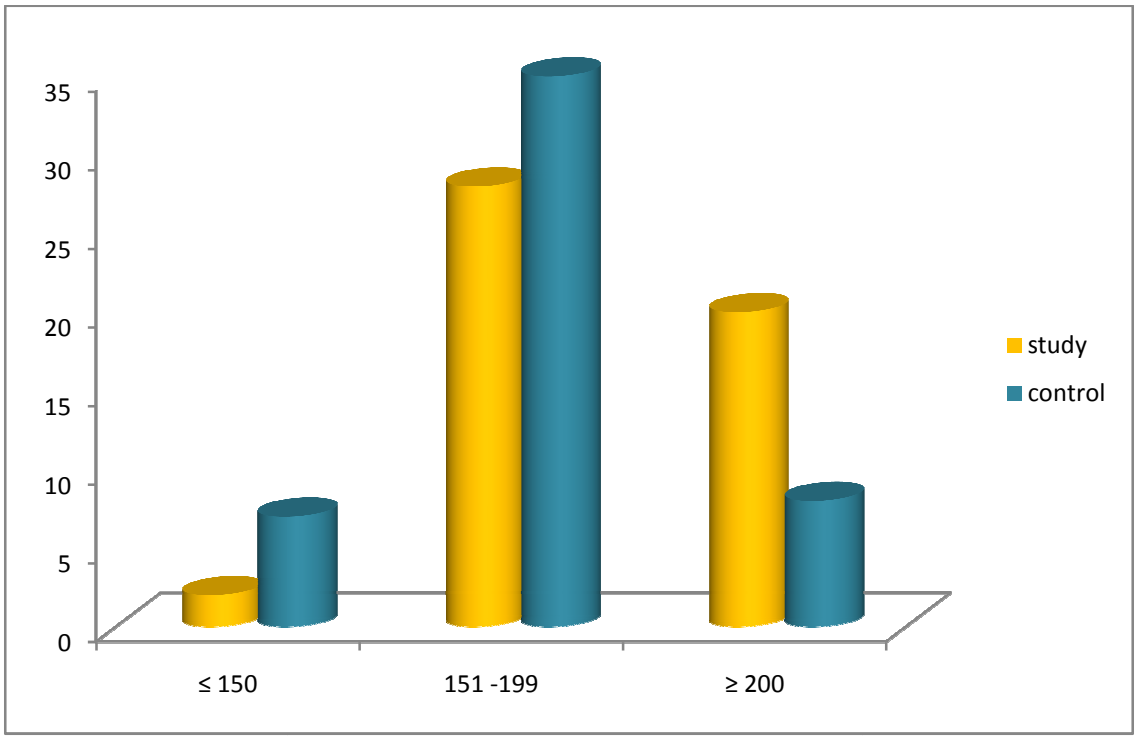


Table-27 Relationship between CIMT with other factors (influencing factors) in study group

CIMT / factor	Co-relation Co-efficient	p-value	Significance	+ve / -ve Co relation
CIMT/ BMI	r = 0.192	>0.05	NS	--
CIMT/ W/ H/ Ratio	r = -0.272	>0.05	NS	--
CIMT/ DBP	r = 0.612	<0.01	S	+ve
CIMT/ SBP	r = 0.778	<0.01	S	+ve
CIMT/ HbA_1C	r = 0.036	>0.05	NS	--
CIMT/ FBS	r = 0.018	>0.05	NS	--
CIMT/ PPBS	r = 0.016	>0.05	NS	--
CIMT/ S.Creatinine	r = 0.22	>0.05	NS	--
CIMT/ TG	r = 0.848	<0.01	S	+ve
CIMT/ LDL-C	r = 0.732	<0.01	S	+ve
CIMT/ HDL-C	r = -0.699	<0.01	S	-ve
CIMT/ Total-C	r = 0.616	<0.01	S	+ve

In the study group, the relationship between CIMT with SBP , DBP, triglycerides, LDL-C ,and total cholesterol are positively correlated ($p<0.01$), which is statistically significant ,Whereas CIMT and HDL-C, the relation is negative correlation, which is statistically significant ($p<0.01$) and CIMT with other factors BMI, Waist hip ratio, HbA1C, FBS, PPBS, S. Creatinine shows correlation, which is statistically not significant ($p>0.05$).

Table-28 Relationship between CIMT with other factors (influencing factors) in control group

CIMT / factor	Co-relation Co-efficient	p-value	Significance	+ve / -ve Co relation
CIMT/ BMI	r = 0.22	>0.05	NS	--
CIMT/ W/ H/ Ratio	r = 0.29	>0.05	NS	--
CIMT/ DBP	r = 0.601	<0.01	S	+ve
CIMT/ SBP	r = 0.764	<0.01	S	+ve
CIMT/ HbA_1C	r = 0.657	<0.01	S	+ve
CIMT/ FBS	r = 0.078	>0.05	NS	--
CIMT/ PPBS	r = 0.065	>0.05	NS	--
CIMT/ S.Creatinine	r = 0.074	>0.05	NS	--
CIMT/ TG	r = 0.699	<0.01	S	+ve
CIMT/ LDL-C	r = 0.787	<0.01	S	+ve
CIMT/ HDL-C	r = -0.699	<0.01	S	--ve
CIMT/ Total-C	r = 0.686	<0.01	S	+ve

In the control group, the relationship between CIMT with TG, LDL-C, total cholesterol and HbA1C, SBP, DBP are positively correlated, which is statistically significant ($p<0.01$). Whereas CIMT with HDL-C is negatively correlated, which is statistically significant. ($p<0.01$) and CIMT with other factors BMI, FBS, PPBS and S. Creatinine shows relationship, which is statistically not significant.

Table-29 Comparing different factors in study and control groups

Factors	Study group Mean± SD	Control Group Mean± SD	t-test	p-value	Significance
DBP	90.8 ± 10.14	84.27 ± 7.37	3.18	<0.001	VHS
SBP	154.4 ± 22.6	133.33 ± 14.4	4.8	<0.001	VHS
HbA_1C	8.15 ± 0.88	7.96 ± 0.64	1.24	>0.05	NS
FBS	155.7 ± 56.2	125.34 ± 14.9	3.68	<0.001	VHS
PPBS	217.2 ± 74.01	168.44 ± 23.45	4.36	<0.001	VHS
S.Creatinine	1.24 ± 0.41	0.98 ± 0.27	3.25	<0.001	VHS
TG	199.86 ± 63.1	140.46 ± 52.1	4.73	<0.001	VHS
LDL-C	138.91 ± 36.11	121.16 ± 49.98	2.09	<0.05	S
HDL-C	39.64 ± 2.84	38.8 ± 5.85	0.23	>0.05	NS
Total-C	193.97 ± 38.7	169.1±45.56	2.55	<0.01	HS

On comparing, various risk factors between study and control groups, statistically very highly significant for CIMT, DBP, SBP, FBS, PPBS, S. Creatinine and triglycerides. Whereas, it is statistically highly significant for BMI and total cholesterol and also, study shows significance for LDL-C. The study showed no statistical significance for age, waist hip ratio, HbA1C and HDL cholesterol.

DISCUSSION

The present cross sectional, case control study was carried out in the department of medicine, Coimbatore medical college hospital, Coimbatore, from July 2014 to June 2015. The patients were grouped into Study (type 2 DM patients with Coronary artery disease) and Control groups (type 2 DM patients without any CAD). The purpose of study was to study carotid intima medial thickness in type 2 diabetes mellitus and to co-relate it with known coronary risk factors.

Distribution of Age & Sex and its correlation with CIMT

In the present study, total number of study cases were 50. Out of which, 30 were male and 20 were female. Whereas, in control group out of 50 cases, 30 were male & 20 were female. Overall mean age in study & control groups was 60.45±11.26 & 58.37±7.85 respectively. On comparison of age in study & control group, t- value is 1.54 and $p > 0.05$ (not significant). Mean age in the present study group is comparable to study conducted by A K Agarwal[56] et al (2008) in which, mean age was 59.78±8.81. Mean age in study group is comparable with studies conducted by Davidson et al[57] which was 58.9±7.8. The mean age in a study done by Shinichi Teno at al[37] was 53.7 yrs, which is lesser than the present study group. In the present study group as the age increased a gradual increase in mean CIMT is noted in both study and control groups.

Table– 30 : Age distribution in relation to CIMT

	Study		Control	
Age	**No.**	**CIMT**	**No.**	**CIMT**
35-44	3	1.05± 0.17	3	0.87± 0.07
45-54	9	1.14± 0.28	10	0.98± 0.33
55-64	17	1.24± 0.34	19	1.01± 0.27
65-74	18	1.26± 0.22	16	1.06 ± 0.08
≥75	3	1.28± 0.16	2	1.12 ± 0.13
Total	**50**	**1.197± 0.35**	**50**	**0.97± 0.30**

On comparing age and CIMT of study group, correlation coefficient 'r' =0.95, $p<0.05$ (statistically significant), whereas in control group correlation coefficient 'r'=0.93, $p<0.05$(significant). Therefore as age increases, CIMT increases, which has a positive correlation and is statistically significant. In Cardiovascular Health Study Daniel H O'Leary et al (1992) [49] studied 5201 patients and concluded that prevalence and severity of carotid atherosclerosis continued to increase with age even in late decades of life. Sang Su Chang et al [58] observed 535 Korean type 2 diabetic patients and found that mean CIMT was positively correlating with age. The present study is very much comparable to the above studies. On comparing gender differences among both study and control groups, higher values of CIMT (CIMT >1mm) is found in 32 patients out of which, 22 are male and 10 are female, suggesting a high CIMT predominantly in male population.

Relation of Diabetes Mellitus and its duration with CIMT

As mentioned earlier in review of literature, Diabetes mellitus and its duration play a significant role in carotid atherosclerosis. The 16 year follow up study in Framingham population by Garcia MJ et al[1] emphasized that there is unique effect of diabetes on Coronary artery disease, which cannot be explained by the associated cardiovascular risk factors. Bonoro et al[16] have studied carotid intima media thickness (CIMT) in a total of 114 patients and concluded that diabetes is characterized by a greater thickness of carotid artery independent of other established risk factors of atherosclerosis. A K Agarwal et al (2008) [56] observed duration of diabetes as a predictor of CIMT, which was statistically proved in his study ($p<0.002$). In the UKPDS 23 study done by R C Turner et al [59] in 1998, they concluded as, the incidence of macrovascular complications in type 2 diabetic patients is twice that of microvascular disease. In the Chennai Urban Population Study (CUPS) done by V Mohan et al[53] in 2000 proved that diabetic subjects have higher intima media thickness values. The present study is very much comparable to above studies, as it showed a positive correlation, that is statistically significant in both study and control groups [correlation coefficient 'r'= 0.823,and 'r'= 0.825, respectively. $p<0.01$(significant)] when duration of diabetes mellitus is compared with progression of CIMT, The mean duration of diabetes in both study and control groups is 6.65± 3.75 and 7.18± 2.78 respectively, which is statistically not significant (student 't'=0.93, $p>0.05$).

Relation of Hypertension with CIMT

In the Cardiovascular Health Study, which consisted of 5201 patients done by Daniel H O'Leary et al [49] observed that SBP and DBP correlated with CIMT, which was statistically highly significant ($p<0.01$). Study done on elderly Finnish diabetic population by Rajala U et al (2003) [60] revealed that, high systolic blood pressure was associated with severe CIMT. A K Agarwal et al[56] in his study showed that SBP and DBP were proved to be predictors of higher than normal mean CIMT ($p<0.05$ and $p<0.017$ respectively). Mean CIMT of hypertensive patients in study group is 1.28±0.25, which is very much higher than mean CIMT of whole study group (1.197±0.35). Also comparing between HTN and non HTN groups in relation with CIMT, it is statistically significant ('t'=2.08, $p<0.05$). On comparison of SBP and DBP between both study and control groups, It is statistically very high significant ($t=4.80$, $p<0.001$ and $t=3.18$, $p<0.001$ respectively). These findings in the present study are consistent with above studies.

Relation of Smoking with CIMT

In the present study, 40% of study group are smokers with mean CIMT (1.37±0.27), which is much higher than non smokers (mean CIMT 1.08±0.32) and smokers of control group (mean CIMT 1.14±0.23). Smokers have higher CIMT compared to non smokers in both groups, which is statistically significant ($p<0.05$). The Cardiovascular study in young Finns study done by Olli T Raitakeri et al(2003) [61] demonstrated that smoking significantly

contributes to atherosclerosis. A Kablak et al[62] in 2004 showed that, smoking was associated with high CIMT. The present study is very much comparable to above studies.

Relation of BMI with CIMT

In the Atherosclerosis Risk in Young Adults (ARYA) study by Anath Oren et al (2003) [65] have done a prospective study and concluded that, increase in BMI is associated with increase in CIMT. Olli T Raitakari et al (2003) [61] measured the coronary risk factors in relation with CIMT, which showed statistical significance between BMI and CIMT. In the present study the mean BMI in study and control group were 25.42±4.74 and 23.19±4.79 respectively, which on comparison had a statistically highly significant association. In the present study,the obese patients (i.e., BMI>25) are more in study group (46%) against only (32%) in control group. Also a very high number of patients with BMI greater than 30 are found in study group (6%) against (2%) in control group.

Relation of Waist Hip Ratio with CIMT

In the present study, mean waist hip ratio of study and control groups is 0.949±0.112 and 0.95±0.044 respectively ($p>0.05$, not significant). The values were comparable with mean values of waist hip ratio in diabetics with and without coronary artery disease (0.9709±0.0728 and 0.9701±0.072 respectively) done in a study by A K Agarwal et al[56]. In the present study, there

is no statistical significance found between increase in waist hip ratio with CIMT ($p>0.05$ in both groups).

Relation of HbA_1C with CIMT

In 2006, Yokoyama Hiroki et al[63] studied around 1578 subjects in type 2 diabetic patients and showed a significant correlation of HbA_1C with rate of CIMT change($p=0.01$). Yamasaki Yoshimitsu et al[64] in 2000 have concluded that, high HbA_1C one of the predictors of progression of carotid IMT in Japanese type 2 diabetic patients. In the present study high HbA1C levels (values greater than 7) indicating a poor control is found in both groups i.e., 90% and 84% in study and control groups respectively.

Relation of Total Cholesterol with CIMT

In 2000, Shinichi Teno et al [37] correlated lipid profile in type 2 diabetic patients with CIMT and concluded that total cholesterol was significantly associated with CIMT. Yamasaki Yoshimitsu et al (2000) [64] concluded that total cholesterol was significantly related to progress of CIMT. In the present study, mean total cholesterol in study and control groups was found to be 193.97±38.74 and 169.1±47.56 respectively. On comparison of total cholesterol with CIMT in study group, which showed statistically positive correlation (correlation coefficient 'r'=0.604, $p<0.01$). In the present control group also shows significant positive correlation, between total cholesterol and CIMT (correlation coefficient 'r'=0.665, $p<0.01$). Therefore the present study is comparable to above studies.

Relation of HDL cholesterol with CIMT

Michael Davidson et al [57] showed the inverse relationship between HDL cholesterol and CIMT by studying the beneficial effect of pioglitazone on HDL cholesterol, which predicted as less progression of CIMT. The mean HDL cholesterol in study and control groups were 39.644± 2.84 and 38.8± 5.85 respectively, which was not significant ($p>0.05$). But in the study group, progression of CIMT had negative correlation with HDL-C (correlation coefficient 'r'= -0.679, $p<0.01$), which is statistically significant. This finding is comparable to above study.

Relation of LDL cholesterol with CIMT

Anath Oren et al [65] in the ARYA study demonstrated that LDL-C was positively associated with significant increase in CIMT. Similar association between LDL-C and CIMT was seen in The Cardiovascular Risk in Young Finns study done by OT Raitakari et al [61] and the ARIC study done by Lloyd Chambless et al[18]. The present study group which showed significant positive correlation ($p<0.01$) between LDL-C and CIMT is very much comparable to above studies. The mean LDL-C in study and control groups is 138.904± 36.11 and 121.166± 49.98 respectively, which is statistically significant ($p<0.05$).

Relation of Triglycerides and CIMT

Shinichi Teno et al (2000) [37] showed a positive correlation between fasting triglycerides and progression of CIMT between ($p<0.05$).A K Agarwal et al (2008) [56] showed that triglycerides are strong predictors of increase in CIMT. In the present study group a positive correlation is found between triglycerides and progression of CIMT (correlation coefficient 'r'=0.839), which is statistically significant ($p<0.01$). The values in control group were very much similar to study group (correlation coefficient 'r'=0.688, $p<0.01$ statistically significant). The mean values of triglycerides in study and control group were 199.86± 63.1 and 140.46± 52.1respectively, which is statistically very highly significant ($p<0.001$). The values are comparable to above studies.

Relation of Serum Creatinine with CIMT

A K Agarwal et al (2008) [56] studied diabetics with and without coronary artery disease and showed that, serum creatinine was positively associated with high mean CIMT($p<0.041$). The present study did not show any significance between serum creatinine and progression of CIMT and it is statistically not significant ($p>0.05$). But there is very high statistical significance observed between study and control groups when serum creatinine is compared to CIMT ($p<0.001$).

Relation of CIMT in diabetic patients with and without Coronary artery disease

The mean CIMT in study group is 1.197±0.35, whereas mean CIMT in control group is 0.97±0.30. On comparison of CIMT between both study and control groups, which shows statistical significance (student't'=3.23, $p<0.01$). A very high mean CIMT is found in all diabetics i.e., both the study and control groups. Mohan et al[53] in the Chennai Urban Population Study (CUPS) in 2000 studied IMT of the carotid artery in South Indian diabetic and non diabetic subjects and observed that the mean IMT value of the diabetic subjects (0.95 ± 0.31 mm) was significantly higher than those of the non-diabetic subjects ($p<0.001$). In a study in 2001 by Jadhav et al[66], an IMT greater than 0.8 mm was observed in CAD patients (whether diabetic only, hypertensive only or both) as against those without CAD. Llyod E Chambless et al[18] in ARIC study proved that prevalence of CIMT of 1mm or more was much higher for those with CAD than without ($p<0.0001$).The findings of present study are very much comparable to the above studies.

SUMMARY

The present cross sectional, case control study was carried out in department of medicine, Coimbatore medical college hospital, Coimbatore.

To summarize the observations in the present study :

- The present study shows that Carotid Intima Media Thickness (CIMT) increases with age, which is a non modifiable risk factor for atherosclerosis and the correlation is statistically significant.

- Higher values of CIMT (>1mm) are found predominantly in male patients in both groups

- The present study emphasized that, as duration of diabetes increases, there is progression of CIMT, which is statistically significant.

- Hypertension an established risk factor for atherosclerosis is found to have a positive correlation with progression of CIMT, which is statistically significant in the present study. Also systolic blood pressure and diastolic blood pressure were statistically significant when compared between both groups.

- In the present study, smoking as an important atherosclerotic factor, which is statistically significant between both the groups. Association of smoking with CIMT, which is also shown to have statistical significance.

- BMI is shown to have statistical significance when compared between both study and control groups, 46% patients in study group had high BMI greater than 25, as against only 32% in control group.

- The findings of the Waist Hip ratio, which is considered an important risk factor for atherosclerosis. but finding of present study not comparable to previous studies and not found to have any statistical significance with CIMT.

- Poor glycaemic levels (HbA1C >7) are found in patients of both study and control groups.

The present study has demonstrated the role of traditional risk factors like total cholesterol, LDL-Cholesterol and triglycerides in the progression of atherosclerosis, as statistically highly significant between the study and control group. There was also positive correlation between these risk factors with progression of CIMT in both study and control groups. But HDL-Cholesterol had a negative correlation with CIMT, which has statistical significance in both the groups.

- In this study, although CIMT is elevated in all patients with type 2 diabetes, a statistically significant high CIMT is found in type 2 DM with Coronary Artery Disease (CAD) as compared to type 2 DM without CAD.

- CIMT along with other coronary risk factors, which is very much increased in the study group when compared with the control group, which is statistically significant. Also comparison of CIMT with other risk factors for atherosclerosis, had proved to be statistically significant.

CONCLUSION

The present, cross sectional , case control study done in Coimbatore medical college hospital , Coimbatore , between July 2014 to June 2015 on Carotid Intima Media Thickness (CIMT) in type 2 diabetics and its correlation with coronary risk factors has concluded that:

- The traditional risk factors for coronary artery disease like Aging , Hypertension, Smoking, Total-Cholesterol, HDL-Cholesterol, LDL-Cholesterol, Triglycerides and Type 2 diabetes with its duration have been shown to have statistical significance with CIMT.

- In the study although CIMT is elevated in all patients with type 2 diabetes, a statistically significant high CIMT is found in type 2 DM with Coronary Artery Disease (CAD) as compared to type 2 DM without CAD.

- This study concludes high Carotid IMT to be a surrogate and reliable marker of higher risk of CAD among type 2 diabetics. The findings of this study clearly shows, the association of CIMT as a reliable factor for judging atherosclerosis with reference to coronary vasculature, it being a simple, non-invasive, safe and cheap screening technique.

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PROFORMA

Name :

Age :

Sex : Occupation : Address:

Date of Admission :

Date of Discharge : IP No. :

Complaints with Duration:

1. Chest pain
2. Pain abdomen
3. Breathlessness
4. Vomiting/ loose motion
5. Excessive sweating
6. Syncope
7. Exertional fatigue
8. Giddiness
9. Oedema feet/ distension of Abdomen/ puffiness of face
10. Palpitation
11. Others

PAST HISTORY:

1. **History of angina pectoris or angina equivalent** Y / N If yes,
   Frequency
   Duration of each attack
   Amount of exertion to produce
   Relieving factor
2. **History of myocardial infarction**
   History of unstable angina
   Medications for the same
3. **History of diabetes mellitus** Y/ N If yes,
   Year of diagnosis
   Mode of diagnosis
   Duration
   Complications at the time of diagnosis
   Patient was taking OHA/ Insulin/ Diet/ All/ None Control of diabetes
4. **History of hypertension** Yes / No , If yes,
   Year of diagnosis
   Mode of diagnosis
   Complications at the time of diagnosis
   Treatment receiving for the same
   Control of HTN
5. **History of other complications of diabetes**
   a) **CNS** - TIA, Major stroke
   b) **PNS** - Peripheral neuropathy
   c) **EYE** - Retinopathy Blurring of vision , Floaters

d) Renal system

Polyuria

Anuria/ oliguria

Fever with chill

Loin pain

Dysuria

e) Peripheral vascular disease

Intermittent claudication

Non-healing ulcer over foot

f) Pulmonary tuberculosis or any other pulmonary infection

g) History of autonomic neuropathy

FAMILY HISTORY:

a) Family History of diabetes

b) Marital status

Spouse diabetic

PERSONAL HISTORY:

a) Smoking Yes / No.
Duration / Amount

b) Tobacco Yes / No
Duration / Amount

c) Consumption of alcoholic beverages Yes / No
Duration /Amount

d) Diet

e) Appetite

f) Bowel habits

g) Weight loss/ weight gain

h) Relevant menstrual / obstetric history in case of females,

i) Any other

GENERAL EXAMINATION:

Height :

Weight :

BMI :

Waist Hip Ratio :

Pallor :

Icterus :

Cyanosis :

Xanthoma :

Sweating :

Engorged veins :

Thyroid :

Clubbing :

Pedal edema :

Others

Vital Signs

PR

BP

RR

Temp

SYSTEMIC EXAMINATION:

Cardio Vascular System:

Pulse

a) Rate
b) Rhythm
c) Volume
d) Character
e) Peripheral pulses Rt / Lt
a) Carotid
b) Superificial temporal
c) Brachial
d) Radial
e) Femoral
f) Popliteal
g) Dorsalis pedis
h) Posterior tibial
i) Radio-femoral delay
j) Vessel wall
k) JVP

EXAMINATION OF CVS:

Inspection

Bulge / retraction / Apical impulse

Abnormal pulsation / Parasternal heave

Engorged vein

Palpation

Apical impulse / Character

Thrills / Parasternal heave

Palpable S_4 (if any)

Percussion (if relevant)

Auscultation

Apex

Tricuspid area

Pulmonary area

Aortic area / Neoaortic area

RESPIRATORY SYSTEM EXAMINATION:

EXAMINATION OF ABDOMEN:

NEUROLOGIC EXAMINATION:

PROVISIONAL DIAGNOSIS:

INVESTIGATION :

ECG

FUNDUS EXAMINATION

HB

TC

DC

ESR

RBS

FBS

PPBS

BLOOD UREA

S-CREATININE

CPK-MB

TROP-I

Lipid profile

Total cholesterol, Triglycerides , HDL-cholesterol , LDL-C

HbA1C

Urine Albumin Sugar Microscopy

Microalbuminuria CXR: (if needed)

Echocardiography

Carotid Intima media thickness (average of left and right)

FINAL DIAGNOSIS

CONSENT FORM

You, Shri./ Smt./ Kum. _____, aged ____ years, S/o / D/o / W/o _____, residing at _____ are requested to be a participant in the research study titled **"*Correlative study of carotid intima media thickness and various coronary risk factors in diabetics with and without coronary artery disease*"** conducted by Dr. SURESH M., one of the post graduate trainees in the Dept. of General Medicine, Coimbatore Medical College and Hospital, Coimbatore. You are eligible for the study as per the inclusion criteria. You can ask any question or seek any clarifications about the study from me before agreeing to participate in this study.

TOPIC OF THE RESEARCH

CORRELATIVE STUDY OF CAROTID INTIMA MEDIA THICKNESS AND VARIOUS CORONARY RISK FACTERS IN TYPE 2 DIABETICS WITH AND WITHOUT CORONARY ARTERY DISEASE

PURPOSE OF RESEARCH

Carotid intima media thickness has been independently associated with coronary artery diseases (CAD) in Indian subjects. There are few Indian studies, where carotid intima- media thickness has been measured

in type 2 diabetics. Therefore the present study was planned to generate more data on this subject with aim of measuring the carotid intima-media thickness in type 2 diabetics with or without CAD, as these patients are more prone to develop early atherosclerosis and macro vascular complications like coronary artery disease. Non invasive procedures like B mode ultrasound of carotid vessel is used and it can predict early atherosclerosis elsewhere in the body, especially coronary atherosclerosis in diabetes patients

PROCEDURES INVOLVED IN THE STUDY

All patients included in this study underwent detailed clinical history, physical examination(systolic and diastolic BP, waist hip ratio, BMI) and necessary investigations (carotid intima media thickness, total cholesterol, high density lipoprotein cholesterol, low density lipoprotein cholesterol, fasting triglyceride, postprandial triglyceride, fasting blood sugar, postprandial blood sugar, serum creatinine, glycosylated haemoglobin)

DECLINING FROM PARTICIPATION

You are hereby made aware that participation in this study is purely voluntary And honorary, and that you have all the rights to decline from participating in it.

PRIVACY AND CONFIDENTIALITY

You are hereby assured that your privacy is respected. Any information about you or provided by you during the study will be kept strictly confidential.

AUTHORIZATION TO PUBLISH RESULTS

Results of the study may be published for scientific purposes and /or presented to scientific groups. In any case, neither will your identity be revealed nor will your privacy be breached.

STATEMENT OF CONSENT

I, _____, do hereby volunteer and consent to participate in this study being conducted by Dr. Suresh M. I have read and understood the consent form (or) it has been read and explained to me thoroughly. I am fully aware of the study details as well as aware that I may ask questions to him at any time.

Signature / Left Thumb Impression of the patient

Station: Coimbatore

Date:

Signature / Left Thumb Impression and Name of the witness

Station: Coimbatore

Date:

ஒப்புதல் படிவம்

பெயர் :

பாலினம் :

முகவரி : வயது :

அரசு கோவை மருத்துவக் கல்லூரியில், பொது மருத்துவதுறையில், பட்ட மேற்படிப்பு பயிலும் மாணவர் **மு.சுரேஷ்** அவர்கள் மேற்கொள்ளும் **"சர்க்கரை நோய் மற்றும் இருதயநோயினால் பாதிக்கப்பட்ட நோயாளிகளை ஒரு தரப்பிலும், சர்க்கரைநோய் மற்றும் இருதய நோயினால் பாதிக்கப்படாத நோயளிகளை மற்றொரு தரப்பிலும் கொண்டு, கழுத்து இரத்தக்குழாயின் தடிமன் மற்றும் பல்வேறு இருதயநோய் காரணிகளை ஒப்பிட்டு பார்க்கும் ஆய்வு"** என்ற சோதனையின் செய்முறை மற்றும் அனைத்து விபரங்களையும் கேட்டுக்கொண்டதுடன், எனது அனைத்து சந்தேகங்களையும் தெளிவுப்படுத்திக்கொண்டேன் என்பதை தெரிவித்துக் கொள்கிறேன்.

நான் இந்த ஆய்வில் முழு சம்மதத்துடனும், சுய சிந்தனையுடனும் கலந்து கொள்ள சம்மதிக்கிறேன்.

இந்த ஆய்வில் என்னுடைய அனைத்து விபரங்களும் பாதுகாக்கப்படுவதுடன், இதன் முடிவுகள் ஆய்விதழில் வெளியிடப்படுவதில் எனக்கு எந்த ஆட்சேபனையும் இல்லை என்பதை தெரிவித்துக் கொள்கிறேன். எந்த நேரத்திலும் இந்த ஆய்வில் இருந்து விலகிக்கொள்ள எனக்கு உரிமை உண்டு என்பதையும் அறிவேன்.

இடம் :

தேதி : **கையொப்பம் / ரேகை**

KEY TO THE MASTER CHART

IP No	:	In patient number
OHA	:	Oral Hypoglycemic Agents
BMI	:	Body Mass Index
W/ H Ratio	:	Waist Hip Ratio
DBP	:	Diastolic Blood Pressure
SBP	:	Systolic Blood Pressure
HbA1C	:	glycosylated Haemoglobin
FBS	:	fasting blood sugar
PPBS	:	post prandial blood sugar
S.creatinine	:	serum creatinine
Total C	:	Total Cholesterol
HDL –C	:	High Density Lipo protein Cholesterol
LDL-C	:	Low Density Lipo protein Cholesterol
TG	:	Triglycerides
CIMT	:	Carotid Intima Media Thickness

MASTER CHART (STUDY GROUP)

S.No	IP. No.	Age	Gender	Symptoms	Duration	Smokers	Insulin	OHA	BMI	W/H/R	DSP	DBP	HbA1C	FBS	PPBS	S. creatinine	Total-C	HDL-C	LDL-C	TG	CIMT
1.	25328	37	M	CP	4	Y	N	Y	19.1	0.89	130	86	6.9	120	166	0.9	220	38.2	164	138	0.86
2.	23884	40	M	SOB	7	N	Y	N	20.2	0.91	146	90	8.2	186	220	1.0	246	39	180	204	0.94
3.	23739	47	M	CP	3	Y	N	Y	17.9	0.94	136	100	9.1	100	170	1.1	196	40.2	176	140	1.24
4.	25261	49	M	SW	6	N	N	Y	27.4	1.01	180	80	8.8	166	180	0.8	230	37	170	138	1.32
5.	30304	51	M	CP	9	Y	N	Y	24.1	0.88	150	86	7.6	110	210	1.2	180	36	136	210	1.14
6.	30339	53	M	CP	2	N	Y	N	32.5	1.08	134	78	7	130	186	1.12	208	41.5	110	166	1.12
7.	30264	56	M	SOB	8	Y	N	Y	21.3	1.1	170	88	7.8	116	148	1.0	166	38.5	138	136	1.16
8.	30384	58	M	CP	3	N	N	Y	25.5	1.06	186	76	8.4	150	178	1.2	248	42	96	172	1.26
9.	33617	60	M	CP	7	Y	N	Y	22.3	0.97	156	96	9.1	164	206	0.7	178	39	112	216	1.18
10.	34964	62	M	SW	2	N	N	N	18.2	0.92	176	74	10.5	120	166	1.0	236	40	140	178	1.3
11.	34946	59	M	CP	6	N	N	Y	26	0.98	138	86	11.2	140	168	1.1	168	38	98	149	1.12
12.	33344	61	M	SW	1	N	Y	N	27	0.86	160	84	6.8	126	226	1.2	250	44	116	220	0.94
13.	33401	63	M	CP	7	Y	N	Y	21.4	1.02	158	82	9.6	130	176	1.0	210	37	180	140	0.88
14.	33258	57	M	CP	4	N	N	Y	29.5	1.01	190	98	8.6	155	227	0.6	252	41	94	180	1.21
15.	33268	64	M	SOB	8	Y	Y	Y	23.4	0.95	136	94	7.8	108	150	1.3	186	38	142	230	1.12
16.	32694	66	M	SW	5	Y	N	Y	28.4	0.96	160	84	8.6	160	182	1.5	238	42.4	93	182	1.08
17.	32711	68	M	CP	9	Y	N	Y	24	0.93	130	100	7	198	230	1.4	166	39.6	190	142	1.14
18.	33261	66	M	SOB	3	N	N	N	27.4	0.9	150	82	8.8	174	190	0.5	260	38.5	97	177	1.4
19.	32680	65	M	CP	10	Y	Y	N	18.3	1.06	132	78	9.6	130	196	1.2	172	41.6	120	144	1.22
20.	32577	70	M	SW	2	N	N	Y	19.7	1.08	160	110	9.8	170	270	1.3	244	37	99	240	1.1
21.	32616	72	M	CP	9	Y	N	Y	22.3	1.13	170	80	6.6	166	200	0.8	212	36	194	144	1.06
22.	28675	71	M	CP	4	N	N	Y	26.8	0.99	156	100	10.3	128	250	1.6	240	43.2	91	140	1.21
23.	27038	69	M	SW	1	Y	N	N	21.5	0.92	166	86	11.2	166	190	0.7	248	34	106	166	1.04
24.	28840	67	M	CP	8	N	N	Y	27.4	0.98	154	76	9.7	118	220	1.7	184	35.5	92	218	1.16

MASTER CHART (STUDY GROUP)

25.	28663	74	M	SOB	3	N	N	Y	29.1	1.12	132	88	9.8	138	167	1.6	218	38	104	155	1.31
26.	28619	73	M	CP	13	Y	N	Y	22.3	1.04	170	74	10.3	136	210	0.8	190	43.2	178	146	0.92
27.	28584	71	M	CP	5	N	N	Y	28.4	0.99	156	90	9.8	116	158	1.8	216	35.5	91	160	1.22
28.	27145	70	M	SOB	12	Y	N	Y	23.5	0.91	180	86	8.7	148	178	0.7	170	34	94	162	1.17
29.	26920	77	M	CP	9	N	N	Y	26.5	0.98	160	84	9.1	156	240	1.5	174	32	117	148	0.96
30.	27169	76	M	SW	4	N	Y	N	24	0.99	136	98	9.7	126	168	1.2	206	42	116	220	0.89
31.	3476	39	F	CP	17	N	N	Y	27.8	0.86	186	96	8.8	168	240	1.4	216	43.5	104	170	0.94
32.	5158	47	F	SOB	2	Y	N	Y	21.6	0.87	158	82	8.1	200	270	0.8	178	40.8	152	186	1.14
33.	8684	49	F	CP	6	N	Y	Y	29.1	0.85	130	70	7.9	128	172	1.3	252	39	98	226	1.22
34.	10628	48	F	CP	3	Y	N	Y	23.7	0.83	166	84	7.8	174	266	0.7	182	36	166	190	0.93
35.	16340	46	F	SW	7	N	Y	N	28.3	0.88	174	76	8.4	156	200	1.8	230	44	120	192	1.32
36.	16372	52	F	CP	1	Y	N	Y	24.3	0.84	138	86	10.4	124	236	0.6	186	43	168	149	1.34
37.	19379	58	F	SW	8	N	N	Y	27.4	0.89	180	98	10.6	178	248	1.1	190	42.5	99	230	1.21
38.	19905	57	F	CP	5	Y	N	Y	19.6	0.91	156	88	9.7	180	200	0.5	260	44	150	184	1.32
39.	19444	59	F	CP	9	N	Y	Y	25.8	0.83	150	78	8.6	156	182	1.9	192	46	124	132	1.06
40.	21102	61	F	SW	7	Y	N	Y	19.9	0.9	132	90	7.8	120	270	0.6	228	51.5	182	130	0.94
41.	25781	63	F	CP	4	N	N	Y	20.8	0.91	190	96	9.4	148	178	1.1	196	38	126	236	0.98
42.	25982	59	F	CP	8	N	N	Y	33.5	0.82	200	80	7.8	114	210	0.8	201	36	122	186	1.18
43.	26307	56	F	SOB	8	Y	Y	N	26.3	0.87	158	100	9.4	144	186	1.8	180	42	139	170	1.22
44.	25777	62	F	CP	7	N	N	Y	23.7	0.88	146	110	10.4	138	220	1.2	248	41	130	220	1.16
45.	27554	68	F	CP	9	N	N	Y	24.2	0.92	180	88	9.6	136	184	1.7	170	47	194	134	1.14
46.	27595	66	F	CP	7	N	N	Y	31.5	0.93	148	86	8.6	180	218	1.1	220	49	96	224	1.06
47.	29927	69	F	SOB	11	N	N	Y	27	0.93	186	98	7.9	174	200	1.6	168	50	187	155	1.22
48.	30367	72	F	CP	8	N	N	Y	22.1	0.87	148	84	8.7	170	220	1.0	210	39	93	160	0.98
49.	30748	74	F	SOB	6	N	N	Y	28	0.88	170	96	8.9	156	176	1.1	164	41	107	232	0.86
50.	30782	76	F	CP	15	N	Y	N	23.5	0.86	176	82	9.4	160	190	1.4	162	46	91	176	1.41

MASTER CHART (CONTROL GROUP)

S.No	IP. No.	Age	Gender	Symptoms	Duration	Smokers	Insulin	OHA	BMI	W/H/R	SBP	DBP	HbA1C	FBS	PPBS	S. creatinine	Total-C	HDL-C	LDL-C	TG	CIMT
1.	34789	39	M	N	3	Y	N	Y	26.8	0.92	142	86	7.2	112	146	1.0	210	42	108	156	0.81
2.	35041	47	M	N	1	N	Y	N	18.2	0.86	130	88	6.8	136	206	1.3	220	36	112	161	0.72
3.	36156	49	M	N	6	N	N	Y	18.7	0.94	150	92	8.2	126	162	1.1	242	41.2	72	86	0.92
4.	36169	46	M	N	12	Y	N	Y	19.6	1.08	132	70	9.1	110	148	1.2	168	38	86	201	0.69
5.	36245	45	M	N	3	N	N	Y	27.2	0.99	168	90	7.6	132	208	1.1	218	41	168	173	0.76
6.	36263	53	M	N	1	N	Y	N	21.2	0.98	120	72	8.5	118	170	1.4	170	39	88	90	0.72
7.	36306	57	M	N	7	Y	N	Y	22.3	0.88	156	74	6.4	116	176	1.2	216	33.6	117	94	0.78
8.	36233	62	M	N	8	Y	Y	Y	23.4	1.02	126	76	9.3	113	180	1.0	136	42	102	102	0.69
9.	36248	61	M	N	17	Y	N	Y	22.5	0.92	124	80	9.9	134	200	0.9	140	38.5	116	158	0.70
10.	35754	59	M	N	1	Y	N	Y	18.3	0.95	146	96	8.6	126	150	0.8	244	43	90	104	0.96
11.	37886	56	M	N	9	N	Y	N	24.9	0.96	130	84	7.0	128	190	0.6	176	36.8	136	163	0.72
12.	37923	55	M	N	2	N	N	Y	22.3	0.98	156	72	9.1	130	186	1.1	222	43.5	76	110	0.81
13.	37930	62	M	N	10	N	Y	Y	28.4	0.99	170	76	8.7	136	210	0.7	163	34.5	202	160	0.69
14.	37939	64	M	N	6	N	Y	N	21.5	0.89	136	82	9.3	112	170	1.2	143	41.6	142	176	0.71
15.	38029	63	M	N	2	Y	N	Y	19.8	1.05	150	80	6.6	122	168	0.8	176	36.8	88	162	0.76
16.	38047	61	M	N	7	N	N	N	29.5	0.97	134	70	7.6	126	156	1.5	228	38	124	126	0.84
17.	38141	67	M	N	14	N	Y	N	20.2	0.87	148	100	8.3	114	148	0.6	128	39.1	118	202	0.68
18.	37883	65	M	N	2	Y	N	Y	22.1	0.98	180	72	6.8	126	162	0.5	132	40	84	166	0.69
19.	38100	66	M	N	3	N	N	Y	18.1	0.94	138	86	9.3	138	206	0.6	246	40	146	136	0.93
20.	38076	69	M	N	8	N	Y	Y	26.8	0.92	156	74	10.1	116	168	0.9	128	40.6	96	164	0.76
21.	36151	71	M	N	5	Y	N	Y	21.3	1.07	132	76	9.8	128	170	0.7	142	39	90	140	0.72
22.	38216	70	M	N	9	N	N	Y	22.5	0.98	120	84	9.6	118	182	1.1	146	41	86	168	0.69
23.	39732	65	M	N	3	N	Y	N	23.6	0.85	124	98	8.5	140	204	0.8	216	36	84	142	0.85
24.	39765	72	M	N	10	Y	N	Y	27.2	0.95	152	80	7.8	130	190	0.7	216	42	137	203	0.86

MASTER CHART (CONTROL GROUP)

25.	39712	70	M	N	4	N	N	Y	24.2	0.96	110	88	9.1	110	196	1.0	152	35	106	78	0.71
26.	39848	71	M	N	6	N	N	Y	28.5	0.90	116	70	8.5	122	182	0.6	232	42.6	82	89	0.92
27.	39840	70	M	N	7	N	N	Y	19.8	0.99	136	72	6.9	113	186	0.8	156	37.3	119	170	0.72
28.	39747	69	M	N	8	Y	N	Y	27.6	0.96	128	76	7.9	123	178	0.9	218	36.2	76	104	0.81
29.	41488	77	M	N	18	N	Y	N	22.5	1.02	156	90	8.6	142	200	1.6	128	34.2	108	155	0.69
30.	41525	76	M	N	9	N	N	Y	23.4	0.95	118	78	7.4	114	166	0.6	126	43.1	78	110	0.70
31.	20752	37	F	N	3	Y	N	Y	32.1	0.87	166	80	7.2	125	158	0.5	128	40.2	162	130	0.71
32.	20621	36	F	N	4	N	N	Y	25.6	0.85	120	82	8.7	110	142	0.7	248	36	80	172	1.06
33.	13385	47	F	N	10	Y	Y	N	18.4	0.86	160	78	7.0	121	178	0.9	230	45	116	172	1.10
34.	13006	45	F	N	5	N	N	Y	24.5	0.91	126	94	10.1	122	166	1.2	230	50	114	204	0.86
35.	12813	50	F	N	6	Y	N	Y	26.6	0.83	178	76	9.3	138	210	0.8	186	42	90	142	0.78
36.	12849	52	F	N	4	N	Y	Y	23.2	0.87	124	72	8.6	110	146	0.6	190	44	128	174	0.79
37.	12023	51	F	N	7	Y	N	Y	22.4	0.84	110	84	7.8	116	170	1.7	210	39.8	92	181	8.01
38.	11959	56	F	N	5	N	Y	N	28.8	0.92	146	70	8.3	120	178	1.0	178	50.2	126	176	0.79
39.	11458	59	F	N	11	N	N	Y	19.8	0.95	116	86	9.4	142	180	0.5	194	38.6	94	168	8.02
40.	10131	57	F	N	8	Y	N	Y	29.6	0.9	128	72	6.7	116	148	0.7	242	44.2	130	184	0.92
41.	9508	55	F	N	4	N	N	Y	20.4	0.87	132	74	10.4	122	186	1.1	166	42.6	96	176	0.86
42.	10165	61	F	N	9	Y	N	Y	21.5	0.82	150	90	11.3	110	166	0.9	154	41.3	130	146	0.75
43.	10202	60	F	N	3	N	N	Y	27.3	0.89	134	80	9.7	116	172	0.7	212	37.4	72	112	0.79
44.	8356	59	F	N	7	N	Y	N	23.6	0.93	128	76	7.6	138	186	0.6	175	36.2	84	186	0.76
45.	8342	63	F	N	5	N	N	Y	22.3	0.92	156	78	8.5	124	189	1.2	168	39.6	86	205	0.70
46.	6521	62	F	N	2	N	N	Y	26.5	0.81	136	80	9.4	128	168	0.8	150	50.6	114	98	0.69
47.	6951	69	F	N	10	Y	N	Y	21.5	0.87	138	88	9.8	117	154	1.0	228	41.3	90	178	0.86
48.	7055	67	F	N	8	N	N	Y	25.8	0.82	158	72	8.7	130	179	0.6	146	42	122	132	0.73
49.	6428	68	F	N	1	Y	N	Y	24.1	0.86	120	74	9.4	128	183	1.1	137	44	96	180	0.72
50.	6380	69	F	N	9	N	N	Y	27.2	0.81	160	80	7.9	117	167	0.5	129	37	78	118	0.68